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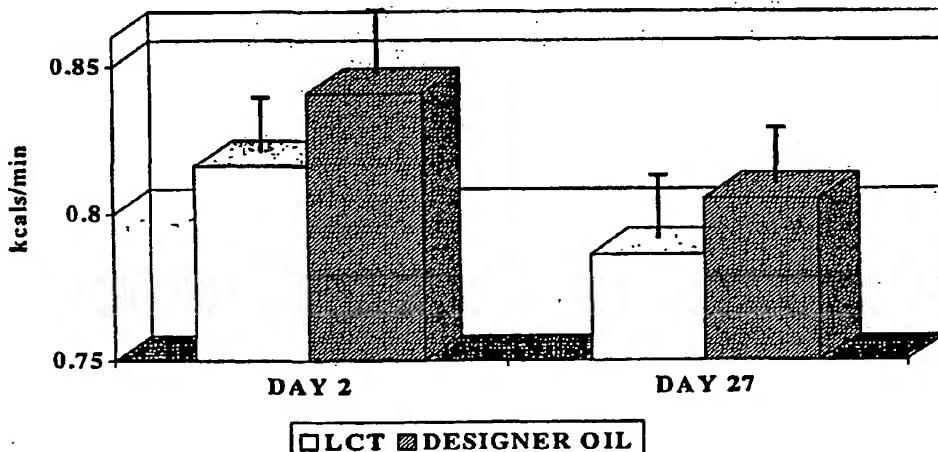
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(54) Title: OIL COMPOSITIONS COMPRISING SHORT, MEDIUM AND LONG CHAIN TRIGLYCERIDES AND USE THEREOF IN REDUCING WEIGHT GAIN

BASAL METABOLIC RATE WITH CONSUMPTION OF A DIET CONTAINING LCT AND DESIGNER OIL



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(57) Abstract: Oil compositions which comprise one or more triglycerides bearing short and medium chain fatty acid residues derived from fatty acids having from 4 to 14 carbon atoms and long chain fatty acid residues derived from fatty acids having from 15 to 22 carbon atoms which are effective in maintaining body weight and controlling weight gain.

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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

OIL COMPOSITIONS COMPRISING SHORT, MEDIUM AND LONG CHAIN TRIGLYCERIDES AND USE THEREOF IN REDUCING WEIGHT GAIN

FIELD OF THE INVENTION

This present invention relates to the field of edible oil compositions and the selective modification of triglyceride chain lengths therein in order to optimize dietary and therapeutic efficacy.

BACKGROUND OF THE INVENTION

The most abundant group of fats and oils are triacylglycerides, or triglycerides formed by the esterification reaction of fatty acids with glycerol, a trihydroxy alcohol. The distinction between fats and oils is arbitrary. At room temperature, a fat is a solid and an oil is liquid. In addition, most triglycerides found in animals are fats, while those in plants tend to be oils.

Fats and oils are the most common lipids and are a major source of dietary energy. They contribute about twice as much energy per weight as carbohydrates or proteins. Fat contributes to the palatability and flavour of food and to the satiety value, since fatty foods remain in the stomach for longer periods of time than do foods containing protein and carbohydrate. Furthermore, fats and oils are carriers of fat-soluble vitamins A, D, E and K as well as essential fatty acids which are important in growth and in the maintenance of numerous body functions. In addition to their role as a fuel or energy source, dietary fats are the building blocks of phospholipids and glycolipids. These

amphipathic molecules are important components of biological membranes.

The fatty acid chains in biological systems usually contain an even number of carbon atoms, typically between 14 and 24, with the 16 (palmitate) and 18 (stearate) carbon fatty acids being the most common. Generally, triglycerides comprised of fatty acid chains with from 2 to 5 carbon atoms are referred to as short chain triglycerides ("SCT") and those with from 6 to 12 carbon atoms are referred to as medium chain triglycerides ("MCT"). Both SCT and MCT are invariably saturated and are found in dairy products as well as some plant oils. Those triglycerides comprised of fatty acid chains with 14 carbon atoms or greater are referred to as long chain triglycerides ("LCT"), may have points of unsaturation and are found in animal, fowl and fish products as well as plant oils.

Metabolically, ingested fats and oils are hydrolyzed into monoacylglycerides, diacylglycerides, fatty acids and glycerol, all of which (with the exception of diacylglycerides) can be absorbed through the intestinal wall. The body then either 1) utilizes these hydrolyzed or partially hydrolyzed fats as raw materials to synthesize its own fats; 2) converts the fatty acids to other compounds such as carbohydrates or cholesterol esters; or 3) converts the fatty acids to energy. Fatty acids are stored within the body in adipose tissue.

Structural differences between MCT versus LCT are responsible for divergent processes of digestion, absorption and transport. For example, short chain fatty acids ("SCFA") and medium chain fatty acids ("MCFA") undergo faster and more complete hydrolysis based on their smaller molecular weight and their capacity to facilitate the action of pancreatic lipase, a key digestive enzyme (1-3). Accordingly, the MCT are more rapidly absorbed into the intestinal lumen as compared to LCT (4). Once absorbed, the mode of transport of fatty acids to the liver and other organs is also chain length dependent. LCT are packaged into chylomicrons and deposited from the lymphatic system into the circulation, passing through the body before reaching the liver (5,6,7). Through this route, long chain fatty acids ("LCFA") have the opportunity to be

picked up by adipose tissue prior to reaching the liver for oxidation. Conversely, SCFA and MCFA travel from the intestine directly to the liver through the portal vein and as such are not exposed to adipose tissue sites prior to hepatic disposal. Consequently, SCFA and MCFA arrive at the liver, a major site of fatty acid oxidation, more quickly than LCFA following a meal.

Triglycerides combining both medium and long chain fatty acid residues, for use in feeding preparations and as nutritional supports are very well known in the art.

US Patent 3,450,818 to Babayan et al. discloses an oil said to be particularly useful for persons having difficulty absorbing fats. The oil comprises triglycerides having a major portion of medium chain (C8:0 and C10:0) fatty acid moieties and a minor portion of essential fatty acids moieties selected from C18 to C20.

US Patent 4,528,197 to Blackburn describes a composition for enhancing protein catabolism in a hypercatabolic mammal. The composition is made of a nutritionally sufficient source of amino acids, carbohydrates and lipids, the latter comprising a controlled triglyceride source, which on hydrolysis, yields both long and medium chain fatty acids.

European Patent Application 201,525 to Jandacek et al. relates to a nutritional fat, suitable for use in enteral and parenteral products, consisting essentially of from about 50% to about 100% by weight of triglycerides having, at the one and three positions, medium chain fatty acid residues with chain lengths of 7 to 11 carbon atoms and at the two position, long chain fatty acid unsaturated residues, preferably linoleic (C18:2), oleic (C18:1) or linolenic (C18:3).

US Patent 5,288,512 to Seiden (The Proctor & Gamble Company) discloses a reduced calorie fat composition comprising at least 15% by weight triglycerides having medium (C6-C10) and long (C17-C26) chain fatty acids and wherein the fat has the following fatty acid composition by weight: a) from 15 to 70% C6-C10 saturated fatty acids; b)

from 10-70% C17 to C26 saturated fatty acids; c) not more than 10% fatty acids selected from either C12:0 and C14:0 and mixtures thereof; d) not more than 20% fatty acids selected from C18:1, C18:2, C18:3 and mixtures thereof; and e) not more than 4% C18:2 fatty acids.

The formation of synthetic triglycerides comprising long and short chain fatty acids residues for use as low calorie fats has also been investigated.

US Patent 5,258,197 to Wheeler et al. (Nabisco, Inc.) describes low calorie triglycerides having both long saturated, preferably C16 to C22 residues and short, preferably C2 to C4 residues. Mixtures of these triglycerides are to be used in edible food compositions, especially fat-based confectionaries, margarine and shortenings. Related patents deriving from the same original application are US Patent 5,378,490 and US Patent 5,662,953.

Despite the fact that there have been developed by researchers numerous low calorie fat products, there remains a commercial need for replacement oils which are efficient in reducing weight gain, maintaining proper body weight and lowering serum lipids.

SUMMARY OF THE INVENTION

The present invention provides a method of reducing weight gain and maintaining a healthy body weight via the enhanced metabolism of fats and decreased energy expenditure in an animal, particularly a human, by administering to the animal an oil composition comprising triglycerides bearing short and medium chain fatty acid residues derived from fatty acids having from 4 to 14 carbon atoms and long chain fatty acid residues derived from fatty acids having from 15 to 22 carbon atoms.

The present invention further provides a method of treating or preventing CVD and its underlying conditions including atherosclerosis, hypercholesterolemia, hyperlipidemia, hypertension, thrombosis, and related diseases such as Type II diabetes, as well as

other diseases that include oxidative damage as part of the underlying disease process such as dementia, ageing, and cancer by administering to an animal one or more triglycerides bearing both short and medium chain fatty acid residues derived from fatty acids having from 4 to 14 carbon atoms and long chain fatty acid residues derived from fatty acids having from 15 to 22 carbon atoms and one or more phytosterols or hydrogenated derivatives thereof.

The present invention further provides a method of reducing serum cholesterol and serum triglycerides in an animal, particularly a human, by administering to the animal one or more of the compositions as described herein.

The present invention further provides oil compositions for use in reducing weight gain and maintaining a healthy body weight via the enhanced metabolism of fats and decreased energy expenditure which comprise one or more triglycerides bearing both short and medium chain fatty acid residues derived from fatty acids having from 4 to 14 carbon atoms and long chain fatty acid residues derived from fatty acids having from 15 to 22 carbon atoms.

In a preferred form of the present invention, the oil compositions additionally comprise one or more phytosterols and/or phytostanols or derivatives thereof. In a further preferred form of the present invention, the oil compositions additionally comprise one or more omega-3 polyunsaturated fatty acids, or derivatives thereof.

The present invention further comprises pharmaceuticals, foods, beverages and nutraceuticals manufactured or supplemented with the oil compositions described herein, for use in reducing weight gain and in maintaining a healthy body weight via the enhanced metabolism of fats therefor.

What is achieved within the scope of the present invention, with the combination of short, medium and long chain fatty acids in the triglycerides, is a positive, heretofore unappreciated, effect on body energy storage and expenditure. The beneficial dietary

effects of the fat and oil compositions of the present invention, including reduced weight gain and maintenance of body weight, cannot simply be attributed to a lower caloric value of these compositions as compared to those the compositions previously investigated comprising either MCT and LCT or SCT and LCT. Rather, it is suspected that these effects are due, at least in part, to the advantages conferred by the combination of MCT and SCT in 1)enhancing total energy expenditure; and 2) altering body composition through the reduction of adipose tissue depots.

The fat and oil compositions of the present invention can be prepared by the selective combination of oil and/or fat products. For example, SCT may be derived from specific fractions of unhydrogenated, partially hydrogenated or fully hydrogenated dairy butterfat, coconut oil, palm kernel oil and the like oils. Sources from which MCT and LCT can be derived are equally available and are described further below. Alternatively, this may be achieved by the formulation and combination of "synthetic" triglycerides having the requisite short, medium and long chain fatty acid moieties. The compositions of the present invention can be used as such or they can be manufactured or incorporated into foods, beverages, dietary supplements, pharmaceuticals and nutraceuticals as described in more detail below.

These and other advantages of the present invention will be become apparent through the entirety of this specification.

BRIEF DESCRIPTION OF THE DRAWINGS

The present invention is illustrated by the following non-limiting drawings in which:

Figure 1 is a bar graph showing the percentage of endogenous oxidation during MCT vs LCT feeding;

Figure 2 is a bar graph showing basal metabolic rate during MCT vs LCT feeding;

Figure 3 is a graph showing the basal metabolic rate with consumption of a diet containing LCT and designer oil

Figure 4 is a graph of Carbohydrate oxidation during basal metabolism with consumption of a diet containing LCT and designer oil

Figure 5 is graph of the net cumulative energy expenditure with LCT and designer oil consumption

Figure 6 is a graph of the net cumulative fat oxidation with LCT and designer oil consumption

Figure 7 is a graph of the net cumulative carbohydrate oxidation with LCT and designer oil consumption

Figure 8 is a graph of the hourly energy expenditure after consumption of a breakfast containing LCT and designer oil (day 2)

Figure 9 is a graph of the hourly fat oxidation after consumption of a breakfast containing LCT and designer oil (day 2)

Figure 10 is a graph of the hourly carbohydrate oxidation after consumption of a breakfast containing LCT and designer oil (day 2)

Figure 11 is a graph of the hourly energy expenditure after consumption of a breakfast containing LCT and designer oil (day 27)

Figure 12 is a graph of the hourly fat oxidation after consumption of a breakfast containing LCT and designer oil (day 27)

Figure 13 is a graph of the hourly carbohydrate oxidation after consumption of a breakfast containing LCT and designer oil (day 27)

Figure 14 is a graph of the thermic effect of a breakfast containing LCT and designer oil (day 2)

Figure 15 is a graph of the thermic effect of food: Fat oxidation after consumption of a breakfast containing LCT and designer oil (day 2)

Figure 16 is a graph of the thermic effect of food: Carbohydrate oxidation after consumption of a breakfast containing LCT and designer oil (day 2)

Figure 17 is a graph of the thermic effect of a breakfast containing LCT and designer oil (day 27)

Figure 18 is a graph of the thermic effect of food: Fat oxidation after consumption of a breakfast containing LCT and designer oil (day 27)

Figure 19 is a graph of the thermic effect of food: Carbohydrate oxidation after consumption of a breakfast containing LCT and designer oil (day 27)

Figure 20 is a graph of the change in body volume compartment after 28 days of LCT and designer oil feeding

Figure 21 is a graph of the change in body volume compartment after 28 days of LCT and designer oil feeding

Figure 22 is a graph of the total cholesterol absolute levels after 28 days of LCT and designer oil feeding

Figure 23 is a graph of the total cholesterol percent change after 28 days of LCT and designer oil feeding

Figure 24 is a graph of the total cholesterol absolute levels after 28 days of LCT and designer oil feeding

Figure 25 is a graph of the LDL-cholesterol percent change after 28 days of LCT and

designer oil feeding

Figure 26 is a graph of the HDL-cholesterol absolute levels after 28 days of LCT and designer oil feeding

Figure 27 is a graph of the HDL-cholesterol percent change after 28 days of LCT and designer oil feeding

Figure 28 is a graph of the HDL-C/LDL-C ratio after 28 days of LCT and designer oil feeding

Figure 29 is a graph of the HDL-C/LDL-C percentage change after 28 days of LCT and designer oil feeding

Figure 30 is a graph of the HDL-C/TC ratio after 28 days of LCT and designer oil feeding

Figure 31 is a graph of the HDL-C/TC percentage change after 28 days of LCT and designer oil feeding

Figure 32 is a graph of the formation of malonaldehyde in designer oil

Figure 33 is a graph of the disappearance of fatty acids of designer oil over 24 hours thermal treatment at 105 C

Figure 34 is a graph of the disappearance of fatty acids of designer oil over 24 hours thermal treatment at 180 C

Figure 35 is a graph showing peroxide values of designer oil following thermal incubation at 180 C.

PREFERRED EMBODIMENTS OF THE INVENTION

According to one embodiment the present invention, there are provided oil compositions for use in reducing weight gain and maintaining a healthy body weight via the enhanced metabolism of fats and decreased energy expenditure which comprise one or more triglycerides bearing short and medium chain fatty acid residues derived from fatty acids having from 4 to 14 carbon atoms and long chain fatty acid residues derived from fatty acids having from 15 to 22 carbon atoms.

In other words, the triglycerides of the present invention are compounds consisting of three molecules of the same or different acids esterified to glycerol (1,2,3-propanetriol) having the formula $(CH_2OH)_2CHOH$. The acids are short and medium (C4 to C14) or long (C15 to C22).

The short chain residues may be either saturated or unsaturated, straight or branched. They may be derived from any synthetic or natural organic acid, including, but not limited to butyric (butanoic), valeric (pentanoic), glycolic(hydroxyacetic), lactic (2-hydroxypropanoic), hydracrylic (3-hydroxypropanoic), hydroxybutyric, hydroxypentanoic and the like acids. As used herein, chemical names include isomeric variations: for example, "butyric acid" includes normal butyric acid (butanoic) and iso-butyric (2-methylbutanoic acid), "valeric acid" includes normal valeric acid and iso-valeric (3-methylbutanoic) as so forth. The preferred fatty acids are butyric or mixtures of these.

Mixtures of short chain fatty acids may be derived from unhydrogenated, partially hydrogenated or fully hydrogenated dairy butterfat, coconut, palm kernel and the like oils.

The medium chain residues are preferably those comprising from 6 to 14 carbon atoms, more preferably from 6 to 10 carbon atoms and most preferably from 8 to 10 carbon atoms. They include, but are not limited to, C6 (caproic acid), C8 (caprylic acid), C10

(capric acid) and C12 (lauric acid) as well as mixtures thereof. The most preferred medium chain fatty chain comprises lipoic or thioctic acid in any one of its forms including alpha-lipoic acid.

The long chain residues may be derived from any synthetic or natural, straight or branched, saturated or unsaturated, organic acid including, but not limited to palmitic (hexadecanoic), stearic (octadecanoic), arachidic (eicosanoic), behenic (docosanoic), lignoceric (tetracosanoic), cerotic (hexacosanoic), montanic (octacosanoic), melissic (triaconanoic) and the like acids. They may also be derived by hydrogenating an unsaturated acid, including, but not limited to palmitoleic (9-hexadecenoic), oleic (cis 9-octadecenoic), elaidic (trans-9-octadecenoic), vaccenic (trans-11-octadecenoic), linoleic (cis, cis-9,12- octadecenoic), linolenic (9,12,15-octadecatrienoic and 6,9,12-octadecatrienoic), eleostearic (9,11,13--octadecatrienoic), arachidonic (5,8,11,14-eicosatetraenoic), nervonic (cis-15-tetracosenoic), eicosapentanoic, docosatetraenoic, docosapentaenoic, docosahexaenoic, and the like acids. Chemical names include isomeric variations.

The long chain residues may be derived from, for example, non-hydrogenated, partially hydrogenated or fully hydrogenated oils such as soybean, safflower, sunflower, high oleic sunflower, sesame, peanut, corn, olive, rice bran, babassu nut, palm, mustard seed, cottonseed, poppyseed, low or high erucic rapeseed, shea, marine, meadowfoam, and the like oils. Alternatively, the long chain residues may be derived from tallow, lard, shea butter, dairy butter, jojoba and mixtures thereof.

Phytosterols/Phytstanols

In a preferred embodiment, the oil compositions of the present invention additionally comprise one or more phytosterols and/or phytstanols or derivatives thereof. It has been found that the presence of the sterol component enhances the overall dietary efficacy of the compositions, particularly in lowering serum cholesterol and serum triglyceride levels.

Phytosterols have received a great deal of attention due to their ability to decrease serum cholesterol levels when fed to a number of mammalian species, including humans. While the precise mechanism of action remains largely unknown, the relationship between cholesterol and phytosterols is apparently due in part to the similarities between the respective chemical structures (the differences occurring in the side chains of the molecules). It is assumed that phytosterols displace cholesterol from the micellar phase and thereby reduce its absorption or possibly compete with receptor and/or carrier sites in the cholesterol absorption process.

The term "phytosterol", within the scope of the present invention, includes all phytosterols without limitation, for example: sitosterol, campesterol, stigmasterol, brassicasterol, desmosterol, chalinosterol, poriferasterol, clionasterol and all natural or synthesized forms and derivatives thereof, including isomers. The term "phytostanol" includes all saturated or hydrogenated phytosterols and all natural or synthesized forms and derivatives thereof, including isomers. It is to be understood that modifications to the phytosterols and phytostanols i.e. to include modified side chains also falls within the purview of this invention. It is also to be understood that, when in doubt throughout the specification, the term "phytosterol" encompasses both phytosterol and phytostanol i.e. the terms may be used interchangeably unless otherwise specified.

The phytosterols and phytostanols for use in forming the compositions of this invention may be procured from a variety of natural sources. For example, they may be obtained from the processing of plant oils (including aquatic plants) such as corn oil and other vegetable oils, wheat germ oil, soy extract, rice extract, rice bran, rapeseed oil, sesame oil and fish oils. Without limiting the generality of the foregoing, it is to be understood that there are other sources of phytosterols and phytostanols such as marine animals from which the composition of the present invention may be prepared. US Patent Serial No. 4,420,427 teaches the preparation of sterols from vegetable oil sludge using solvents such as methanol. Alternatively, phytosterols and phytostanols may be obtained from tall oil pitch or soap, by-products of forestry practises as described in US

Patent Serial No. 5,770,749, incorporated herein by reference. Phytosterols and phytostanols are widely available through commercial supply companies.

Without limiting the generality of the foregoing, it is to be understood that there are numerous known methods of extracting and purifying phytosterols and phytostanols from the "source" of choice and the present invention is not limited to any one method of attaining these purified phytosterols and phytostanols.

Omega-3 Polyunsaturated Fatty Acids

In a yet another embodiment, the oil compositions of the present invention additionally comprise one or more omega-3 polyunsaturated fatty acids ("omega-3 PUFA's) or derivatives thereof. It has been found that the presence of the omega-3 PUFA's in the animal diet favourable reduces circulating levels of triglycerides and possible total and LDL cholesterol levels. It has also been found that consumption of diets rich in omega-3 PUFA's results in reduced platelet aggregation and accordingly a reduced tendency for blood clots.

The omega-3 PUFAs (C18:3n3) for use within the composition of the present invention are selected from alpha-linolenic acid, EPA and DHA in the form of, inter alia, fatty acids, triglycerides, phospholipids, esters or free fatty acid salts.

In one embodiment of the present invention, the omega-3 PUFAs may be extracted from zooplankton, fish or other marine animals using suitable bioconcentration techniques. In the alternative, omega-3 PUFAs may be synthesized using microalgae as the source material. In one preferred form, marine fish oil may be mixed directly with SCT and MCT components to form a composition of the present invention. The marine oil may be extracted by techniques known in the art from, inter alia: finfish such as cod, salmon, tuna, herring, halibut, shark, catfish, pollock, dogfish, anchovy, mackerel, trout, and eel; animals such as seals and whales; crustaceans such as crabs, clams and lobster; mollusks and the like.

Without limiting the generality of the foregoing, the most preferred marine sources of omega-3 PUFAs are as follows:

Source	Grams, Omega-3/100 calories*
salmon (sockeye)	1.71
tuna	1.22
salmon (pink)	1.15
shark (spiny dogfish)	1.14
halibut	1.13
anchovy	1.10
salmon (Atlantic)	1.08
mackerel (Atlantic)	1.08
salmon (Pacific)	1.03
spanish sardine	0.91
trout (rainbow)	0.86
mackerel (Pacific)	0.85
swordfish (herring)	0.75

* 8

Alternatively, plant sources of omega-3 PUFAs may be used. The great advantage of plant sources may be reduced odour as compared to some marine sources. Plant sources include, but are not limited to, plant oils such as hemp oil, flaxseed oil linseed oil and corn oil as well as soy. The most preferred plant-derived sources are flax seed oil and linseed oil.

Process Preparing Composition

The compositions of the present invention may be prepared by a variety of methods which would be apparent to those skilled in the art, and this disclosure is not intended to be limited to any one. Nonetheless, in the spirit of full and complete disclosure, the

following processes are suggested:

- 1) In one embodiment, the specific triglycerides forming the compositions of the present invention may be prepared using synthetic procedures known to those skilled in the art, such as, for example, directly esterifying glycerol or glycerol esters with fatty acids, using fatty acid halides (notably chlorides) or fatty acid anhydrides, transesterifying glycerol with fatty acid esters, or interesterifying short, medium and long chain triglycerides for such a time and under such conditions that triglycerides bearing the described chain residues form. Starting materials for the triglycerides (the fatty acids and glycerols) may be obtained commercially or isolated from natural sources.
- 2) In another embodiment, the preferred short, medium and long chain triglycerides may be isolated from natural or processed fats or oils, or fractions thereof using techniques known in the art.

"Designer" Oils

Within the scope of the present invention, what is essentially achieved is the formation of oil compositions which maximize dietary and therapeutic efficacy. As described in more detail below, one use of these compositions is in reducing weight gain, maintaining body weight and lowering serum lipids and triglycerides in animals, particularly humans, without necessarily decreasing caloric intake, as taught by the heretofore published "modified" fats.

The compositions of the present invention can be prepared having many ratio of triglyceride chain lengths. When the triglycerides of the present invention are prepared "synthetically", as described further below, they can comprise any combination of short, medium and long acids from 0 to 100% by weight of any of the three. In one preferred form, the triglycerides comprise roughly from 33 to 67 mole % of short chain residues, 33 to 67 mole % of medium chain residues and 33 to 67 mole % of long chains fatty acid residues.

In another preferred form, the short and medium chain residues collectively comprise from 30 to 70% by weight of total fatty acids present in the oil composition, with long chain residues comprising the balance. Even more preferably, these long chain residues are selected from C18:1n9, C18:2n6 and C18:3n3 and are derived from one or more of olive oil, linseed oil and flaxseed oil.

With respect to dosage, although other ratios and concentrations are fully within the purview of the present invention, (i.e. the invention is not to be limited to the concentrations disclosed) it is preferred that the composition of this invention comprise, in a form for daily administration to humans, up to up to 3 grams of phytosterols and/or phytostanols and up to 5 grams of omega-3 PUFAs (all based on administration to a 70 kg individual). In another preferred form, the composition is prepared in a form to provide from 0.5 to 2.5 grams of phytosterols and/or phytostanols and from 2.5 to 5 grams of omega-3 PUFAs for daily consumption. In a most preferred form, the composition comprises 1.7 grams of each component. For example, if phytosterols are added to provide 1.7 grams in total in 50 grams of oils or fat, this is the equivalent of 3 to 5% phytosterols by weight. Similarly, if 2.5 to 5 grams of omega-3 PUFA are to be provided, they should be added to the composition at 5 to 10% by weight. It will also be recognized that the provision of much larger daily doses of the constituents of the compositions are not harmful to the animal host, as excess will simply pass through normal excretory channels.

Advantages and Uses of the Compositions

Obesity is an important risk factor for cardiovascular disease ("CVD"), the latter being the most common cause of mortality and morbidity in Western societies. Obesity also influences other risk factors for CVD including hypertension, hypertriglyceridemia, and hypercholesterolemia. What the preferred compositions of the present invention have achieved is a simultaneous approach for controlling obesity, and CVD by replacing the dietary consumption of LCT with SCT and MCT in order to promote a negative energy

balance. Ultimately, this promotion of negative energy balance would be useful also for non-obese individuals.

By mechanisms which are as yet not completely understood, the compositions of the present invention result in decreased weight gain, possibly due to the fact that MCT and SCT undergo different metabolic processing during digestion, absorption, transport and partitioning for oxidation than LCT. SCT and MCT are more readily absorbed into the intestinal lumen as compared to LCT (4). Once absorbed, SCT and MCT travel directly from the intestine to the liver through the portal vein and do not by-pass adipose tissue sites. In addition, the promotion of weight loss by the compositions of the present invention can perhaps be explained (although this invention is not limited to any one proposed mechanism of action) by preliminary findings which suggest that the rate of fat oxidation (both endogenous and exogenous) is increased following MCT feedings (refer to Figure 1)

Figure 1 shows the results of studies in which subjects consumed MCT vs LCT-based diets over a period of 14 days each, and endogenous fat oxidation was measured on day 14. Figure 1 shows that the consumption of MCT resulted in greater endogenous oxidation as compared to LCT. It is believed that the presence of SCT may work in synergy with these MCT effects: MCT and SCT combined result in increased endogenous fat oxidation. The increase in endogenous fat oxidation which is afforded by the compositions of the present invention has important implications in the treatment and prevention of obesity. As obesity can be defined by an excess amount of adipose tissue, any intervention that can result in even a gradual reduction in the amount of adipose tissue can have enormous implications for long-term weight balance.

Figure 2 shows the results of the study above on the basal metabolic rate ("BMR") of the subjects. It is clear, even in this preliminary study, that extended feeding of MCT for up to 14 days results in increased BMR. Again, it is believed that the presence of SCT works in synergy with these MCT effects: MCT and SCT combined result in an even greater increase in BMR, resulting in decreased adipose tissue stores (and weight loss)

through adipose immobilization as a result of increased energy expenditure.

What is most important to note regarding the compositions of the present invention is that the combination of SCFA, MCFA and LCFA in the triglycerides results in a more negative energy balance (for example, more fat oxidized than ingested) in the individual than if the same number of calories were ingested in the form of LCT. This has not been appreciated until now. In other words, the compositions of the present invention do not rely, as is clearly shown in the prior publications, on the creation of compounds or compositions having reduced calories or "lower-fat" in order to achieve the desired goal of weight reduction. The goals of weight reduction and maintenance are achieved without sacrificing caloric value of the diet.

In a most preferred form, the fat or oil compositions of the present invention additionally comprise one or more phytosterols and/or phytostanols or derivatives thereof in order to increase serum HDL cholesterol, decrease serum LDL cholesterol. In a further preferred embodiment, the fat or oil compositions of the present invention additionally comprise one or more omega-3 PUFA's in order to decrease serum triglycerides.

Methods of Use

The compositions of the present invention may be used directly and without further modification in cooking, baking and the like as agents to prevent weight gain and regulate proper body weight in humans and to lower serum cholesterol and triglycerides. They may be added to any other edible oil or fat and used for cooking, baking, and general use. Alternatively, the compositions may be treated to enhance delivery into various other delivery media. For example, the composition may be physically modified as described in International Application No. PCT/CA99/00402, specifically pages 11-23, (published on November 25, 1999 and incorporated herein by reference) to enhance even further the solubility and dispersability of the components in the chosen delivery medium.

In addition, the present invention fully contemplates the formation of oleaginous gel foodstuffs such as peanut butter, mayonnaise, ice cream and margarine spreads incorporating such compositions. Further, the compositions can readily be included in the manufacturing of a variety of low fat foods. There are numerous modes or "vehicles" of delivery of this composition, accordingly, this invention is not intended to be limited to the following delivery examples.

1) Pharmaceutical Dosage Forms:

It is contemplated within the scope of the present invention that the compositions of the present invention may be incorporated into various conventional pharmaceutical preparations and dosage forms such as tablets (plain and coated) for use orally, buccally or lingually, capsules (hard and soft, gelatin, with or without additional coatings) powders, granules (including effervescent granules), pellets, microparticulates, solutions (such as micellar, syrups, elixirs and drops), lozenges, pastilles, ampuls, emulsions, microemulsions, ointments, creams, suppositories, gels, and transdermal patches, modified release dosage forms together with customary excipients and/or diluents, adjuvants and stabilizers.

The compositions of the present invention, adapted into the appropriate dosage form as described above may be administered to animals, including humans, orally, by injection (intra-venously, subcutaneously, intra-peritoneally, intra-dermally or intra-muscularly), topically or in other ways.

The compositions as described herein may be used in both dietary and therapeutic capacities in order to treat and/or prevent CVD, its underlying conditions such as hypercholesterolemia, hypertriglyceridemia, arteriosclerosis, hypertension, thrombosis, related diseases such as Type II diabetes, as well as other diseases that include oxidative damage as part of the underlying disease process such as dementia, aging, and cancer. In populations, which are considered "high-risk" for CVD or any of the oxidation related disorders, it is contemplated that the compositions and foodstuffs in which they are contained be used in primary, secondary and tertiary treatment

programs.

2) Foods/Beverages/Nutraceuticals:

In another form of the present invention, the compositions of the present invention may be incorporated or manufactured into foods, beverages and nutraceuticals, including, without limitation, the following:

- 1) Dairy Products --such as dairy beverages, shakes and dairy mixes;
- 2) Fat-Based Products--such as margarines, spreads, mayonnaise, shortenings, cooking and frying oils and dressings;
- 3) Baking Products;
- 4) Confectioneries--such as chocolate, candies, chewing gum, desserts, non-dairy toppings (for example Cool Whip), sorbets, icings and other fillings;
- 5) Beverages-- emulsions; dietary supplement and meal replacement drinks such as those sold under the trade-marks Boost and Ensure; and
- 1) Miscellaneous Products--including eggs and egg products, processed foods such as soups, pre-prepared pastas

The compositions of the present invention may be incorporated directly and without further modification into the food, nutraceutical or beverage by techniques such as mixing, infusion, injection, blending, dispersing, emulsifying, immersion, spraying and kneading.

The doses of the compositions of the present invention, comprising the SCT, MCT and LCT and optional components such as phytosterol, are listed in preferred form hereinabove but will vary depending upon, among other factors, the mode of delivery

(i.e. how and into which food or beverage or pharmaceutical the compositions are ultimately incorporated), the patient size and condition, the result to be achieved, as well as other factors known to those skilled in the art of food additives and medicinal agents.

While the following examples are intended to illustrate various aspects of the present invention and to assist in the preparation of the compositions, they are not intended to limit the scope of invention as claimed herein.

EXAMPLE 1

Study of Respiration and Oxygen Consumption after 28 days of MCT and LCT feeding
Goal: To determine if long term feeding of MCT and LCT has an effect on energy expenditure, fat and carbohydrate oxidation and respiratory quotient ("RQ") in obese women.

Fifteen women (BMI 28-35 kg/m²) were randomized to either MCT or LCT-containing diets for a period of 28 days, after a 2 month wash out period . Energy expenditure was measured 30 minutes before breakfast and for 30 minutes from each hour for five hours after breakfast on days 2 and 27 of each experimental period. On day 2, basal RQ was lower (p<0.05) with MCT consumption than with LCT consumption but there was no significant effect of diet during the post-prandial period. On day 27, RQ was lower (p<0.01) with MCT consumption than with LCT consumption 3 hours after breakfast, but was greater (p<0.05) than with LCT consumption at 5 hours. The rate of oxygen consumption was not influenced by dietary fat type on day 2 but on day 27, it was greater with MCT consumption than LCT consumption after breakfast (p<0.01). The rate of carbon dioxide excretion was greater with MCT consumption than LCT consumption 5 hours after breakfast on day 2 (p<0.05), and at 1 and 2 hours post-breakfast on day 27 (p<0.05).

From these results it can be concluded that long term MCT consumption reduces RQ and increases oxygen consumption in obese women.

EXAMPLE 2**COMPARISON OF MCT/PLANT STEROL "DESIGNER OIL" VS LCT OIL ON ENERGY EXPENDITURE, BODY COMPOSITION AND BLOOD LIPID PROFILE OF OVERWEIGHT WOMEN**

Goal: To determine if consumption of a "Designer Oil" in accordance with the present invention which is rich in SCT and MCT and plant sterols, compared with a control LCT, influences (i) longer term body composition, (ii) energy expenditure and (iii) plasma lipid profile in overweight individuals.

Twenty-three healthy, normolipidemic, overweight females with a BMI of greater than or equal to $28\text{kg}/\text{m}^2$ were recruited for the study. All subjects were screened through interview for absence of chronic illness including diabetes, hypertension, cardiac, hepatic, renal, and gastrointestinal dysfunction, as well as for contraindication for MRI scanning, prior to entrance into the study. Exclusion criteria included the use of lipid-lowering drugs, beta-blockers or diuretics, and a personal history of cardiovascular disease. Those reporting exercise of more than 5 times per week, or undergoing pregnancy and lactation were excluded from the study. Screening total cholesterol and triglyceride levels were required to be within normal ranges (total cholesterol <7.0mmol/L and TG <3.0mmol/L). Seventeen subjects completed the entire study.

Experimental diets (refer to Table I for macro and micronutrient compositions of diets) consisted of nutritionally adequate prepared North American solid foods. The diets were composed of 45% of energy as carbohydrate, 15% as protein, and 40% as fat. Of

the dietary fat, 75% was delivered as either a combination of MCT oil, butter and coconut oil to increase the proportion of MCT, olive oil to increase the level of monounsaturated fatty acids, and flaxseed oil to provide a desirable level of n3-polyunaturated fatty acids, or as beef tallow as a source of LCT. Non-fat constituents of the diets were identical across diets. Diets were designed to contain over 40% of fatty acids as C12:0 or shorter for the MCT diet and over 50% of the fatty acid as C18 or longer for the LCT diet. In the experimental "Designer Oil" diet, Phytrol (Forbes Medi-Tech Inc.) was administered at a level of 2.2mg/kg body weight/day, in order to regulate circulating cholesterol levels. The experimental diets were based on a three-day rotating cycle menu to provide variety and were served as three equicaloric meals per day.

Adjustment of nutrient intake to individual subject energy requirements was done using the Mifflin equation 9, to which an activity factor of 1.7 was multiplied to compensate for additional energy needs of active adults. Body weight was monitored daily before breakfast during both treatment phases to ensure constant body weight. During the first week of phase 1, caloric intake was readjusted by increments or decrements of 2% in case of losses or gains in body weight, in order to provide a weight maintaining diet. Energy levels were fixed after that point and were identical during both dietary treatment cycles. The fatty acid composition of both diets is reported in **Table 2**.

Subjects were tested using a randomized crossover design, with two 28-day dietary feeding cycles separated by a 4- or 8-week washout period. Subjects were randomly

assigned to dietary treatment and the number of subjects per dietary treatment per cycle was balanced. During the washout period, subjects consumed their habitual diets. Using the present protocol, each subject was tested during the same phase of her menstrual cycle. On days 1 and 28 of each treatment cycle, subjects were weighed upon rising. Subjects' body composition was measured using MRI scanning procedures to provide an integral three-dimensional image of fat, fat free and bone tissue compartments. From these images, precise measurements of body compartment volumes were made. Differences in body composition between days 1 and 28 were computed. Midway through the dietary cycle, a 3-day fecal collection was completed to assess the fraction of energy consumed, which was not absorbed. On the morning and early afternoon of days 2 and 27, basal metabolic rate and the thermic effect of food were assessed using respiratory gas exchange. Fasting circulatory lipid levels were determined on days 1, 26 and 28 of each dietary phase to evaluate the impact of the present designer oil on lipid status.

Magnetic Resonance Imaging (MRI) Technique for Measurement of Human Body

Composition:

Of the methods used to measure body composition, MRI is the most accurate and precise for assessment of changes in body composition derived from small nutritional perturbations (10).

Body composition measurements using MRI were conducted on days 1 and 28 of each dietary cycle. This resulted in a total of 4 MRI scanning sessions per subjects. Tissues

from each scanned image were identified using a colouring system that allowed the program to discriminate between the various tissue compartments for calculation of their individual areas. Calculation of the tissue area of respective regions was then accomplished by summing up the given tissues' pixels and multiplying by the pixel surface area. A series of truncated pyramids were then created based on successive image scans and three-dimensional volumes of fat and fat free masses calculated. From these calculations, precise volume determinations were produced for each type of tissue, yielding the total fat and fat free mass of each subject during each scan.

Measurement of Total Daily Energy Expenditure Using Energy Intake Balance:

Energy intake was constant and known as subjects were fed as inpatients. Fat lost through the feces was determined through fecal collection and lipid extraction analyses conducted from days 13 to 15 of each dietary phase. Therefore, energy absorbed was determined as the difference between energy intake, energy lost in the feces and expended as measured using DeltaTrac metabolic monitor (Sensormedics, Anaheim, California). Any increases or decreases in body tissue compartments, as determined through MRI, represent energy stored or lost, respectively. Because of the law of conservation of energy expenditure, any energy absorbed that is not stored must be expended or energy expended above amount of energy absorbed represents energy released from storage compartments.

Determination of Basal Metabolic Rate and Thermic Effect of Food:

On study days 2 and 27 of each phase, subjects' basal metabolic rate and subsequent

6-hour thermogenic response to a standardized breakfast meal was measured upon waking. A DeltaTrac metabolic monitor was utilized to determine oxygen consumption and carbon dioxide production, both expressed at standard temperature and pressure, in each subject. To achieve this, a ventilated hood was placed over the subjects' heads with Collins tubing connecting the hood to the monitor. Following a 30min warm-up period, the DeltaTrac analyser was calibrated using a standard reference gas. Respiratory gas exchange measures were carried out for 30 minutes in each subject shortly after rising for assessment of basal metabolic rate. Data were collected over the last 20 minutes of this period and minute-by-minute oxygen consumption and carbon dioxide production rates determined and converted into energy equivalents using the de Weir equation (11). Subjects then consumed a breakfast meal containing the appropriate treatment fat and 33% of their calculated energy needs, and then returned under the hood for six more periods of 30 minutes each to assess the thermic effect of the breakfast meal. A 6hr period has been found necessary for capturing the rise to peak of TEF, particularly when subjects are consuming LCT based diets . Minute by minute respiratory exchange data was converted to energy equivalents, as described above, and presented as average minute energy expenditure or substrate oxidation. The thermic effect of food was calculated as the difference between post-meal and basal metabolic rate measures at each 30min time point following the breakfast meal. During the days on which respiratory gas exchange measures were made, consumption of the lunch meal was delayed until following the completion of the indirect calorimetry measurement.

Measurement of Plasma Cholesterol and Triglyceride Levels:

Blood samples were drawn after a 12hr overnight fast, collected in EDTA-containing Vacutainer tubes and centrifuged for 15 minutes at 1500 rpm to separate plasma from red blood cells (RBC). Both fractions were stored at -80°C until analysis. All tubes were coded by an external party to blind investigators for analysis and data compiling procedures. Plasma total (TC) and HDL-C as well as triglyceride levels were analyzed in quadruplicate with standardized reagents using a VP Autoanalyser (Abbott Laboratories, North Chicago, IL, USA. The cholesterol reference method was used to allow direct comparison of fresh specimen samples with the Canadian Reference Laboratory Ltd (1996) (Vancouver, BC, Canada). Measurement of HDL-C in plasma was done after precipitation of apolipoprotein B with dextran sulfate and magnesium chloride (12). LDL-C levels were calculated using the Friedewald equation (13) based on values for TC and HDL-C, as well as triglycerides.

Calculation of Sample Size:

Sample size estimates and associated power were assessed using the one sample t-test statistical tables of Machin and Campbell (14). Sample size was estimated on ability to detect a change in body composition using MRI attributable to the dietary fat type provided. Our previous data have demonstrated that dietary shifts in fat from an SCT and MCT to LCT blend result in a projected elevation of total energy expenditure by 160 Kcal/d.

Data Production and Statistical Analysis:

For each subject, data was obtained at the beginning and end of each feeding period for (i) body fat free and fat masses and their respective volumes, (ii) basal metabolic rate and thermic effect of food for 6 hours post-prandially and (iii) total, LDL, and HDL cholesterol and TG levels.

Data are expressed as means \pm standard deviation.

Results

Of a total of 23 women recruited into the study, 17 successfully completed both experimental phases.

Figures 3 and 4 compare basal metabolic rate, and carbohydrate oxidation, respectively, with consumption of the designer oil and the LCT diet on days 2 and 27. BMR with consumption of the designer oil diet was 0.8410.0822 kcals/min on day 2 and 0.8050.110 kcals/min on day 27 and 0.8160.105 kcals/min with consumption of the LCT diet on day 2 and 0.7860.0756 kcals/min on day 27. Average cumulative EE, fat oxidation, and carbohydrate oxidation with consumption the designer oil and LCT diet on days 2 and 27 are shown in **Figures 5-7**, respectively. There was no difference between the diets for any of the parameters on day 2. On day 27, EE was significantly greater ($p<0.01$) with consumption of the designer oil diet compared to the LCT diet. EE on the designer oil diet was 0.9530.100 kcals/min and 0.9030.0798 kcals/min on the LCT diet. Fat oxidation on day 27 was also significantly greater ($p<0.05$) with consumption of the designer oil diet (0.07970.0107 g/min) versus the LCT diet (0.07530.00900 g/min). There was a significant effect ($p<0.01$) of diet on energy

expenditure and fat oxidation and a significant effect ($p<0.01$) of day on energy expenditure. Neither of these factors was significantly affected by carbohydrate oxidation. Hourly variations in EE, fat oxidation, and carbohydrate oxidation are shown in **Figures 8-10** for day 2 and **Figures 11-13** for day 27. Differences between post-meal EE, fat oxidation and carbohydrate oxidation and basal values are shown in figures 14-16 for day 2 and 17-19 for day 27. TEF fat and carbohydrate oxidation were both significantly affected ($p<0.01$) by diet but not by day.

Average fecal fat excretion values are given in **Table 3**. Consumption of the designer oil diet resulted in significantly greater ($p<0.05$) total lipid excretion than did consumption of the LCT diet. However, considering that the designer oil diet contained 22 mg phytosterol/kg body weight and that dietary phytosterols are largely excreted in the feces, then net fat excretion on the designer oil diet becomes non-existent. Therefore, fatty acid excretion was significantly greater ($p<0.01$) with consumption of the LCT diet than the designer oil diet.

Total body compartment volumes are shown in **Figures 20 and 21**. There was no significant difference in changes in body compartment volumes after consumption of the designer oil diet compared to consumption of the LCT diet.

Supplementation of the LCT diet resulted in a mean total cholesterol level of 4.801 ± 0.843 mmol/L for the average of days 26 and 28 of the study, while the designer oil diet significantly decreased those levels to 4.366 ± 0.809 mmol/L ($p=0.0001$, **Figure**

22). The designer oil diet resulted in a negative 5.207% variation in TC between baseline and endpoint values, and the LCT group experienced a positive 0.683% variation in TC (**Figure 23**). Hence, the net effect of the designer oil diet was a negative 5.811% variation in total cholesterol levels, when adjusted for the LCT diet, but this difference expressed as a percentage was not found statistically significant ($p=0.0525$, **Table 4**).

The "designer oil" diet significantly decreased LDL-cholesterol levels from 2.658 ± 0.585 to 2.369 ± 0.624 mmol/L ($p=0.0233$, **Figure 24**) in baseline and endpoints values respectively, which is equivalent to a 10.893% lowering in this parameter (**Figure 25**). On the other hand, the beef tallow based diet resulted in a non-significant 3.672% positive variation in LDL-cholesterol (**Figure 25**), from 2.743 ± 0.486 mmol/L at baseline to 2.844 ± 0.675 mmol/L after 28 days (**Figure 24**). Significant differences were found when the absolute changes in LDL-cholesterol between day 1 and endpoints ($p=0.0341$), and when the endpoints alone ($p=0.0001$) were compared between dietary treatments. The net effect of the phytosterol-containing designer oil diet on LDL-cholesterol levels was a significant 14.452% decrease after the effect of the LCT diet was accounted for ($p=0.0173$, **Table 4**).

Plasma levels of HDL-cholesterol were found unchanged following either diet. Starting levels of this parameter were 1.329 ± 0.307 and 1.287 ± 0.315 mmol/L in the LCT and designer oil groups respectively; and following treatment, mean concentrations of 1.318 ± 0.295 and 1.322 ± 0.318 mmol/L were found in the LCT and designer oil groups, respectively (**Figure 26**). A trend toward an increase in HDL-cholesterol of 2.777% in

amplitude was found subsequent to the designer oil supplementation, and a slightly negative variation of 0.838% subsequent to LCT; however, these changes were not significant (**Figure 27**).

The ratio of HDL to LDL-cholesterol was found favorably increased following designer oil consumption, from 0.495 ± 0.104 at baseline to 0.582 ± 0.147 after 28 days ($p=0.0114$, **Figure 28**). The LCT diet resulted in a non-significant negative variation in this ratio, from 0.489 ± 0.122 at day 1 to 0.481 ± 0.122 at the mean of days 26 and 28 (**Figure 28**). Comparison of the diets according to both the absolute changes in the ratio of HDL to LDL-cholesterol between day 1 and endpoints ($p=0.0121$), and the endpoints alone ($p=0.0013$) showed significant difference. A net positive variation of 19.357% was found in the HDL:LDL-cholesterol ratio, when substituting the LCTdiet for the designer oil diet; this parameter was not significantly different when expressed as a percentage (**Table 4**).

Ratios of HDL to total cholesterol were also found positively influenced by the designer oil diet, increasing from 0.278 ± 0.041 to 0.304 ± 0.051 mmol/L ($p=0.0126$) on the experimental versus undergoing a slight negative non-significantly variation from 0.279 ± 0.048 to 0.276 ± 0.043 mmol/L on the LCT diet (**Figure 30**). Comparison of the diets according to both the absolute changes in HDL:TC ratios between day 1 and endpoints ($p=0.0190$), and the endpoints alone ($p=0.0033$) showed significant difference. The switch from a LCT to designer oil enriched diet resulted in a positive 10.510% variation in the cardiovascular disease protective ratio of HDL-C:TC (**Table 4**).

Discussion

Results obtained in this study show greater EE and fat oxidation with designer oil composition than with LCT consumption. This study further shows that this difference becomes accentuated, rather than attenuated after 27 days of consumption. From the fecal sample analyses, it was observed that the totality of the fat consumed during the designer oil phase was absorbed. During consumption of the "designer oil" diet, subjects retained, on average, 32 kcals less than during consumption of the LCT diet. This would lead to a deficit of 864 kcals over the 27-day feeding period, which would be equivalent to a difference in body weight of approximately 0.11 kg between the designer oil phase and the LCT phase.

The present experiment has provided evidence to suggest that supplementation of a designer oil composed of MCT, phytosterols and n3-PUFA for a period of 28 days positively influences the cardiovascular risk profile in healthy normolipidemic overweight women. The atherogenic LDL-cholesterol, being of most concern in the development of heart disease, has been found significantly reduced by as much as 14.452% over a month's period. Moreover, total cholesterol was reduced when looking at endpoints across treatment groups. No significant reduction in total cholesterol was found when looking at the absolute difference between baseline and endpoints compared between groups; this may due to the already low occurring levels of TC in the present study subjects at baseline, which do not allow for an extensive decline in TC levels over the

course of 28 days. However, a greater decrease in TC in normolipidemic subjects would not be necessary nor desirable in clinical settings. Since levels of HDL-cholesterol were found unchanged following both diets, the ratios of HDL:LDL and HDL:TC, important in the evaluation of the cardiovascular risk profile, have been found positively influenced by the designer oil diet. Even though the observed decline in cholesterol can only be attributed to the combination of dietary factors tested herein, most of the effect is likely due to the presence of phytosterols. The anticipated increase in cholesterol levels following MCT consumption has not been observed in the present settings; hence, our results agree with a neutral or possibly slight cholesterol raising effect of MCT.

The greatest concern from the cardiovascular disease perspective when utilizing MCT as weight-maintaining agents is the anticipated large increase in plasma triglyceride levels. Avoiding this was done by combination of MCT with the triglyceride-lowering n3-PUFA, obtained by addition of flaxseed oil to the diet. The 8.775% negative variation in TG caused seen after consumption of a precisely controlled weight maintaining diet providing 3 equicaloric meals per day, and being restricted from alcohol, was not significant. The MCT containing designer oil did not show equivalent lowering in TG but an apparent non-significant 4.154% increase was reported. These observations were not of statistical relevance and, therefore, our designer oil did not worsen the triglyceridemic state of the normolipidemic overweight women studied. However, the observed variations must still be considered since consumption of the designer oil may not be beneficial to hypertriglyceridemic subjects. A significant decline in TG levels may be achieved by incorporation of marine n3-PUFA, which are better established as

triglyceride-lowering agents.

In conclusion, consumption of the present designer oil composed of MCT, phytosterols and n3-PUFA for a period of 28 days, as part of a precisely controlled weight-maintaining diet, favorably influenced the cardiovascular risk profile of healthy, normolipidemic, overweight women. Also, the significant differences observed in EE and fat oxidation between the designer oil diet and the LCT diet are quite encouraging. These results show that without reducing the amount of energy required to maintain body weight in healthy individuals, subjects could lose 1.5kg of body weight per year when shifting from a diet containing LCT as its main source of fat to a diet containing mostly the MCT based formulation of the present invention.

Table 1. Macronutrient and Micronutrient Composition of the Diets

<u>Breakdown of Dietary Fat</u>	Designer Oil	LCT ("Control")	
Saturated Fat (% fat)	63.66	50.77	
Monounsaturated Fat (% Fat)	24.69	41.98	
Polyunsaturated Fat (% Fat)	11.72	7.26	
P:S ratio	0.18	0.14	
<u>Essential Nutrients</u>			
n-3 Fas (g)	6.11	1.13	1.10
n-6 Fas (g)	9.52	8.55	7.0
n-6:n-3 ratio	1.56	7.57	4 to 10
Folate (ug)	402	416	185
Vitamin B6 (mg/g protein)	0.025	0.027	0.015
Vitamin B12 (ug)	4.1	4.5	1.00

Table 2. Fatty Acid Composition of the Diets

Fatty Acid	Designer Oil Diet	LCT Control Diet
C6:0	0.10	0.03
C8:0	19.44	0.06
C10:0	23.60	0.17
C12:0	3.87	0.26
C14:0	2.64	3.36
C14:1	0.18	0.62
C15:0	0.15	0.39
C16:0	10.10	26.13
C16:1	0.85	2.75
C18:0	3.76	20.37
C18:1n-9	23.66	38.61
C18:2n-6	7.14	6.41
C18:3n-3	4.58	0.85

Table 3. Average daily fecal fat excretion values.

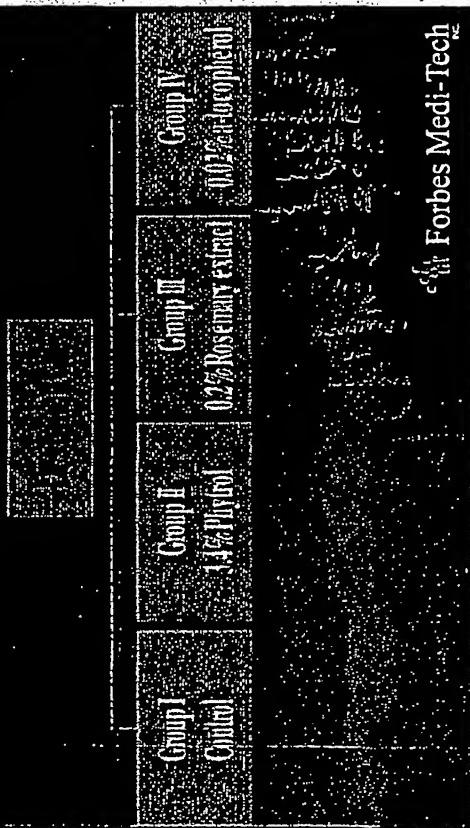
Diet	Mean (SD)
LCT (g)	1.089 (0.691)
MCT (total lipid) (g)	1.716 (1.364)
MCT (total lipid-phytosterol intake) (g)	-0.0769 (1.356)

Table 4. Blood Lipid Parameters

	Designer Oil (Mean d26&28)	LCT (Mean d26&28)	% Difference (from LCT to Designer)
Total Cholesterol (mmol/L)	4.366 ± 0.809 a (ab: P=0.0001)	4.801 ± 0.843 b	-5.811 (P=0.0525)
Triglyceride (mmol/L)	1.420 ± 0.566	1.373 ± 0.550	13.156
HDL-Cholesterol (mmol/L)	1.322 ± 0.318	1.318 ± 0.295	3.583
LDL-Cholesterol (mmol/L)	2.369 ± 0.624 c (cd: P=0.0001)	2.884 ± 0.675 d	-14.452 * (* : P=0.0173)
HDL-C / LDL-C ratio	0.582 ± 0.147 e (ef: P=0.0013)	0.481 ± 0.122f	19.357
HDL-C / TC ratio	0.304 ± 0.051 g (gh: P=0.0033)	0.276 ± 0.043 h	10.510

Table 5

**THE STUDY ON THE OXIDATIVE
STABILITY OF DESIGNER OIL**



Forbes Medi-Tech

EXAMPLE 3

Study of the Thermal Stability of the "Designer Oil" of the Present Invention

This study investigated the oxidative stability of the designer oil composition of the present invention. The designer oil alone was the control. In each case, rosemary, a phytosterol composition (called Phytrolä) or vitamin E was additionally provided. It is clear from Figures 32 through 35 that the preferred composition of the present invention, which is the combination of designer oil and phytosterols, provides the greatest anti-oxidant effect and thermal stability for the product.

Table 5 outlines the study groups. Figures 32-35 shows the results in graph form.

REFERENCES

1. Clement J. Digestion and absorption of dietary triglycerides. *J Physiol* 1976; 72:137-170
2. Fernando-Warnakularsuriya GJ et al. Studies on fat digestion, absorption, and transport in the suckling rat. I: Fatty acid composition and concentrations of major lipid components *J Lipid Res.* 1981;22:668-674
3. Mascioli EA et al Serum fatty acid profiles after intra-venous medium chain fatty acid administration. *Lipids* 1989;24:793-798
4. Caspary WF Physiology and pathophysiology of intestinal absorption. *Am J. Clin Nutrition* 1992;55S:299S-308S
5. Bloom IL et al Participation of phospholipids in lymphatic transport of absorbed fatty acids. *J. Biol. Chem* 1951;189:261-268
6. McDonald GB et al. Portal venous transport of long-chain fatty acids absorbed from rat intestine. *Am J. Physiol* 1980;239:G141-G150
7. Vallot A et al. Influence of diet on the portal and lymph transport of decanoic acid in rats Simultaneous study of its mucosal metabolism. *Comp Biochem Physiol A* 1985;82:693-699

8. The Omega Connection: the facts about fish oils and human health S.K. Niazi, Health Sciences Centre. University of Illinois at Chicago, Esquire Books Inc, Chapter 13.

11. MacDougall DE, Jones PJH, Vogt J, Phang PT, Kitts DD. Utilization of myristic and palmitic acid in humans fed different dietary fats. *Eur J Clin Invest* 1996;26:755-762.
9. Mifflin MD, St Jeor ST, Hill LA, Scott BJ, Daugherty SA, Koh YD. A new predictive equation for resting energy expenditure in healthy individuals. *Am J Clin Nutr* 1990;51:241-7.
10. Fowler PA, Fuller MF, Glasbey CA, Foster MA, Cameron GG, McNeill G, Maughan RJ. Total and subcutaneous adipose tissue in women: the measurement of distribution and accurate prediction of quantity by using magnetic resonance imaging. *Am J Clin Nutr* 1991;54:18-25.
12. Warnick GR, Benderson J, Albers JJ. Dextran sulfate-Mg²⁺ precipitation procedure for quantitation of high-density-lipoprotein cholesterol. *Clin Chem* 1982;28:1379-1388.
13. Fiedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. *Clin Chem* 1972;18:499-502.
14. Machin D, Campbell MJ. Statistical tables for the design of clinical trials. Blackwell Scientific Publications. Oxford, London pp. 83-85.

WE CLAIM:

1. A method of reducing weight gain and maintaining proper body weight via the enhanced metabolism of fats and decreased energy expenditure in an animal, particularly a human, consists of administering to the animal an oil composition comprising triglycerides bearing short and medium chain fatty acid residues derived from fatty acids having from 4 to 14 carbon atoms and long chain fatty acid residues derived from fatty acids having from 15 to 22 carbon atoms.
2. The method of claim 1 wherein the medium chain fatty acid residues have from 6 to 10 carbon atoms.
3. The method of claim 1 wherein the medium chain fatty acid residues have from 8 to 10 carbon atoms.
4. The method of claim 1 wherein the triglycerides are derived from a source selected from the group consisting of unhydrogenated dairy butterfat, partially hydrogenated dairy butterfat, fully hydrogenated butterfat, coconut oil, palm kernel oil, soybean oil, safflower oil, sunflower oil, high oleic sunflower oil, sesame oil, peanut oil, corn oil, olive oil, rice bran oil, babassu nut oil, palm oil, mustard seed oil, cottonseed oil, poppyseed oil, low or high erucic rapeseed oil, shea oil, marine oil, meadowfoam oil, tallow, lard, shea butter, dairy butter, jojoba, mixtures thereof and non-hydrogenated, partially hydrogenated and fully hydrogenated derivatives thereof.
5. The method of claim 1 wherein short and medium chain residues comprise from 30 to 70% by weight of the total fatty acids present in the oil composition, with long chain residues comprising the balance.
6. The method of claim 5 wherein the long chain residues are selected from the group comprising C18:1n9, C18:2n6 and C18:3n3 and are derived from one or more of olive

oil, linseed oil and flaxseed oil.

7. A method of lowering serum cholesterol and triglycerides in an animal, particularly a human, which comprises administering to the animal an oil composition comprising:

a) one or more triglycerides bearing short and medium chain fatty acid residues derived from fatty acids having from 4 to 14 carbon atoms and long chain fatty acid residues derived from fatty acids having from 15 to 22 carbon atoms; and

b) one or more phytosterols, or hydrogenated derivatives thereof.

8. The method of claim 7 wherein the medium chain fatty acid residues have from 6 to 10 carbon atoms.

9. The method of claim 7 wherein the medium chain fatty acid residues have from 8 to 10 carbon atoms.

10. The method of claim 7 wherein the triglycerides are derived from a source selected from the group consisting of unhydrogenated dairy butterfat, partially hydrogenated dairy butterfat, fully hydrogenated butterfat, coconut oil, palm kernel oil, soybean oil, safflower oil, sunflower oil, high oleic sunflower oil, sesame oil, peanut oil, corn oil, olive oil, rice bran oil, babassu nut oil, palm oil, mustard seed oil, cottonseed oil, poppyseed oil, low or high erucic rapeseed oil, shea oil, marine oil, meadowfoam oil, tallow, lard, shea butter, dairy butter, jojoba, mixtures thereof and non-hydrogenated, partially hydrogenated and fully hydrogenated derivatives thereof.

11. The method of claim 7 wherein short and medium chain residues comprise from 30 to 70% by weight of the total fatty acids present in the oil composition, with long chain residues comprising the balance.

12. The method of claim 11 wherein the long chain residues are selected from the group comprising C₁₈:1n9, C₁₈:2n6 and C₁₈:3n3 and are derived from one or more of olive oil, linseed oil and flaxseed oil.

13. The method of claim 7 wherein the composition additionally comprises one or more omega-3 polyunsaturated fatty acids, or derivatives thereof.
14. The method of claim 7 wherein the phytosterol is selected from the group consisting of sitosterol, campesterol, stigmasterol, brassicasterol, desmosterol, chalinosterol, poriferasterol, clionasterol, all natural or synthesized forms and derivatives thereof, including isomers and all hydrogenated derivates thereof.
15. An oil composition for use in maintaining proper body weight via the enhanced metabolism of fats and decreased energy expenditure in an animal, particularly a human, comprises triglycerides bearing short and medium chain fatty acid residues derived from fatty acids having from 4 to 14 carbon atoms and long chain fatty acid residues derived from fatty acids having from 15 to 22 carbon atoms
16. The composition of claim 15 additionally comprising at least one phytosterol.
17. The composition of claim 15 additionally comprising a phytosterol selected from the group consisting of sitosterol, campesterol, stigmasterol, brassicasterol, desmosterol, chalinosterol, poriferasterol, clionasterol and all natural or synthesized forms and derivatives thereof, including isomers.
18. The composition of claim 15 additionally comprising at least one phytostanol.
19. The composition of claim 15 additionally comprising a phytostanol selected from the group consisting of all saturated or hydrogenated phytosterols and all natural or synthesized forms and derivatives thereof, including isomers.
20. The composition of claim 15 wherein the triglycerides are derived from a source selected from the group consisting of dairy butterfat, coconut oil, palm kernel oil soybean oil, safflower oil, sunflower oil, high oleic sunflower oil, sesame oil, peanut oil,

corn oil, olive oil, rice bran oil, babassu nut oil, palm oil, mustard seed oil, cottonseed oil, poppyseed oil, low or high erucic rapeseed oil, shea oil, marine oil, meadowfoam oil, tallow, lard, shea butter, dairy butter, jojoba, mixtures thereof and non-hydrogenated, partially hydrogenated and fully hydrogenated derivatives thereof.

21. The composition of claim 15 wherein the medium chain fatty acid residue has from 6 to 10 carbon atoms.

22. The composition of claim 15 wherein the medium chain fatty acid residue has from 8 to 10 carbon atoms.

23. The composition of claim 15 wherein short and medium chain residues comprise from 30 to 70% by weight of the total fatty acids present in the oil composition, with long chain residues comprising the balance.

24. The composition of claim 15 wherein the long chain residues are selected from the group comprising C18:1n9, C18:2n6 and C18:3n3 and are derived from one or more of olive oil, linseed oil and flaxseed oil.

25. The composition of claim 15 wherein the triglycerides comprise from 33 to 67% by weight of short chain fatty acid residues, from 33 to 67% by weight of medium chain fatty acid residues and from 33 to 67 % by weight of long chain fatty acid residues.

26. The composition of claim 15 additionally comprising one or more omega-3 polyunsaturated fatty acids, or derivatives thereof.

27. A product therapeutically effective at reducing weight gain and maintaining proper body weight via the enhanced metabolism of fats in an animal and at treating and preventing cardiovascular disease and, in particular its' underlying conditions atherosclerosis, hypertriglyceridemia and hypercholesterolemia, which comprises:

a) one or more triglycerides bearing short and medium chain fatty acid residues derived

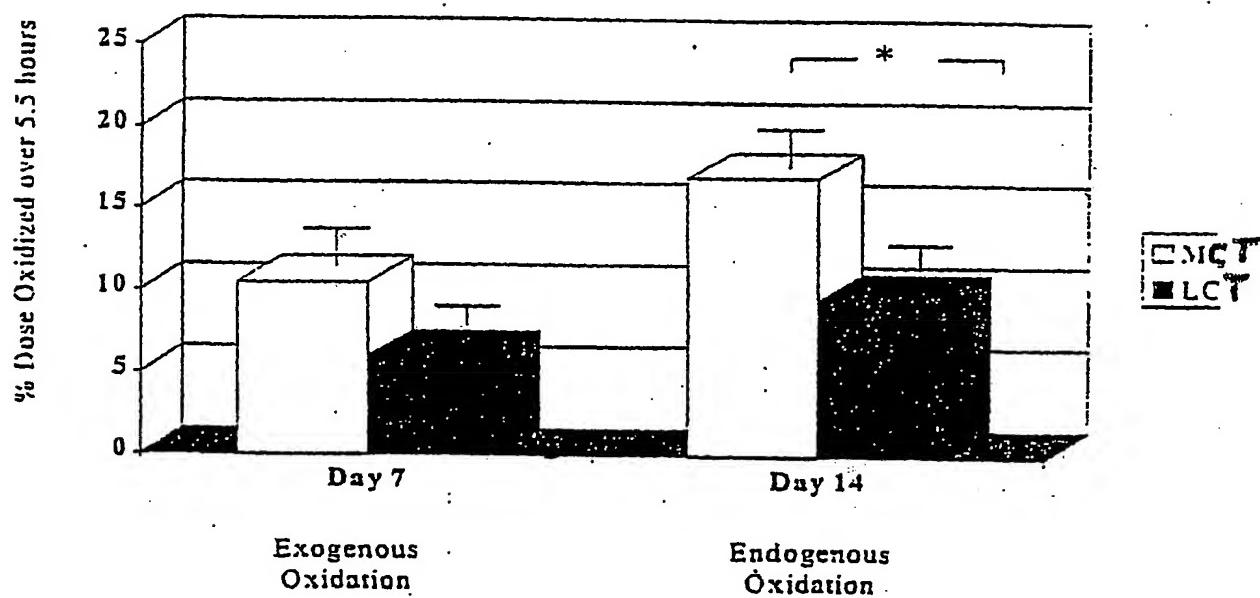
from fatty acids having from 4 to 14 carbon atoms and long chain fatty acid residues derived from fatty acids having from 15 to 22 carbon atoms; and

- b) one or more phytosterols or hydrogenated derivatives thereof; and
- c) a pharmaceutically acceptable or food-grade carrier therefore.

20. A comestible or beverage comprising the composition of claim 15.

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Figure 1. Endogenous Oxidation During MCT vs. LCT Feeding



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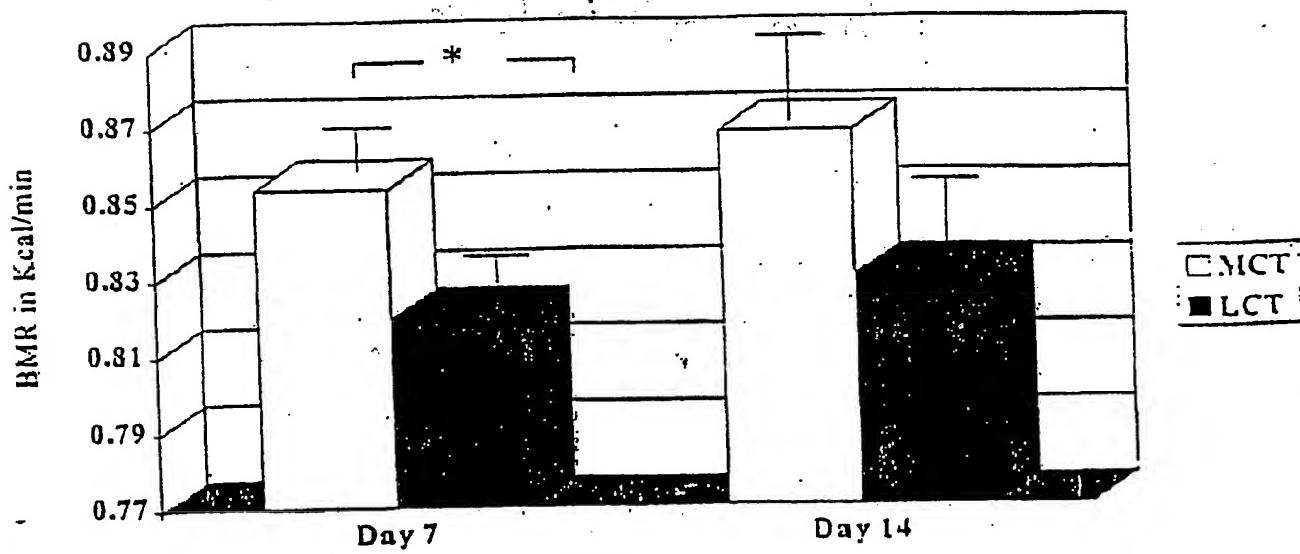
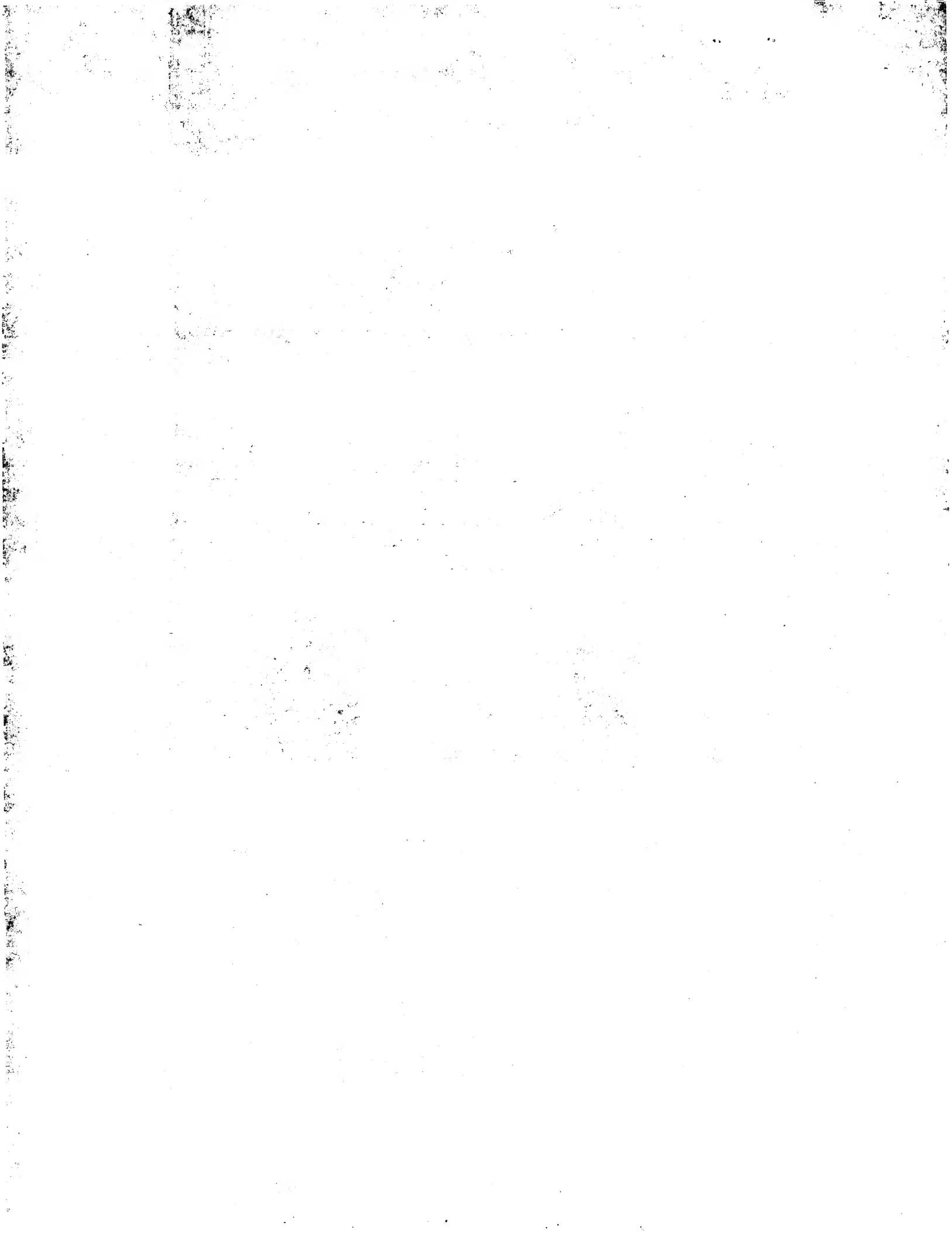
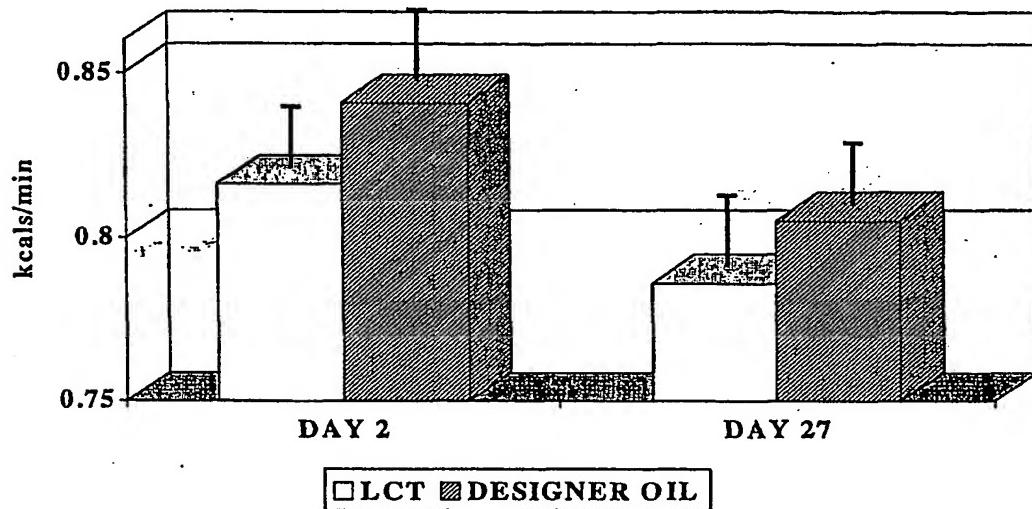
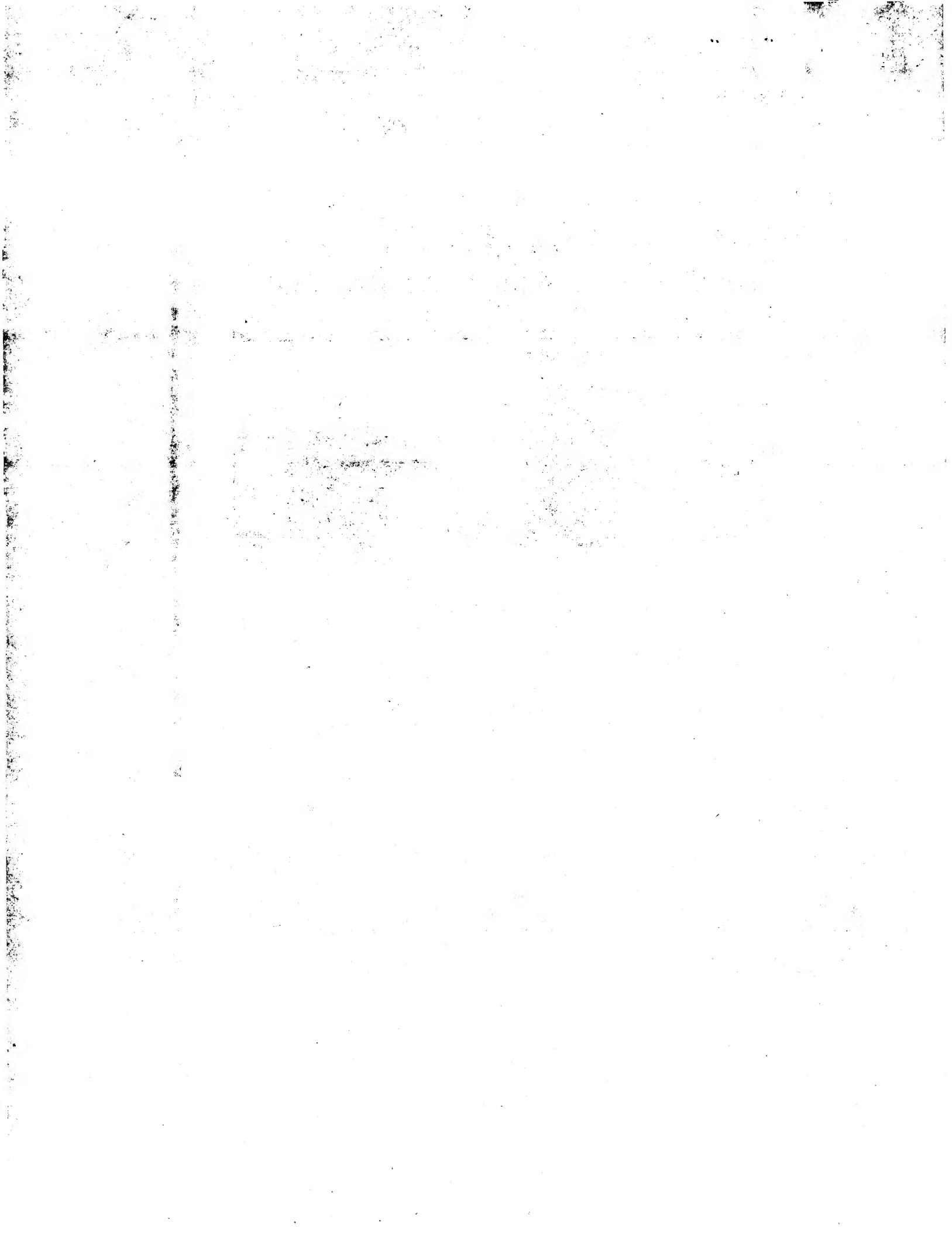


Figure 2. Basal Metabolic rate during MCT vs. LCT Feeding

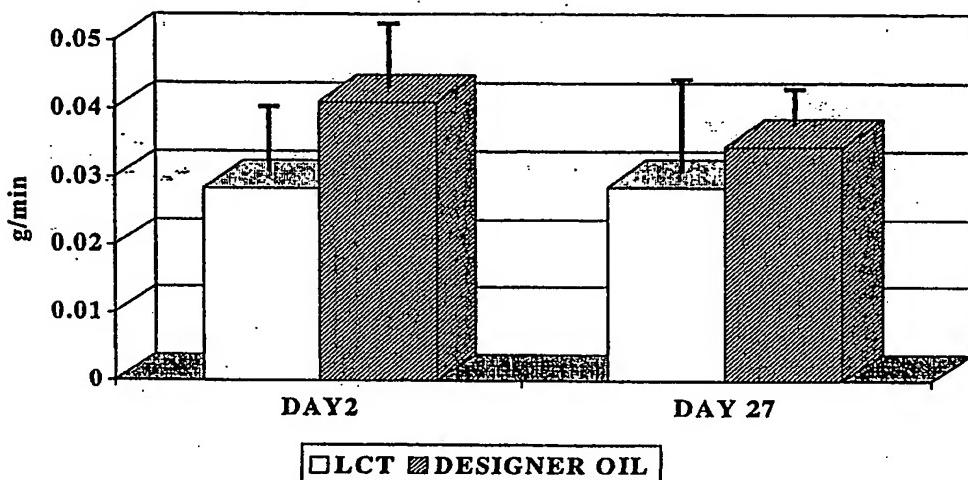


3
Figure 2. BASAL METABOLIC RATE
WITH CONSUMPTION OF A DIET
CONTAINING LCT AND DESIGNER OIL





4
Figure 4. CARBOHYDRATE OXIDATION
DURING BASAL METABOLISM WITH
CONSUMPTION OF A DIET
CONTAINING LCT AND DESIGNER OIL



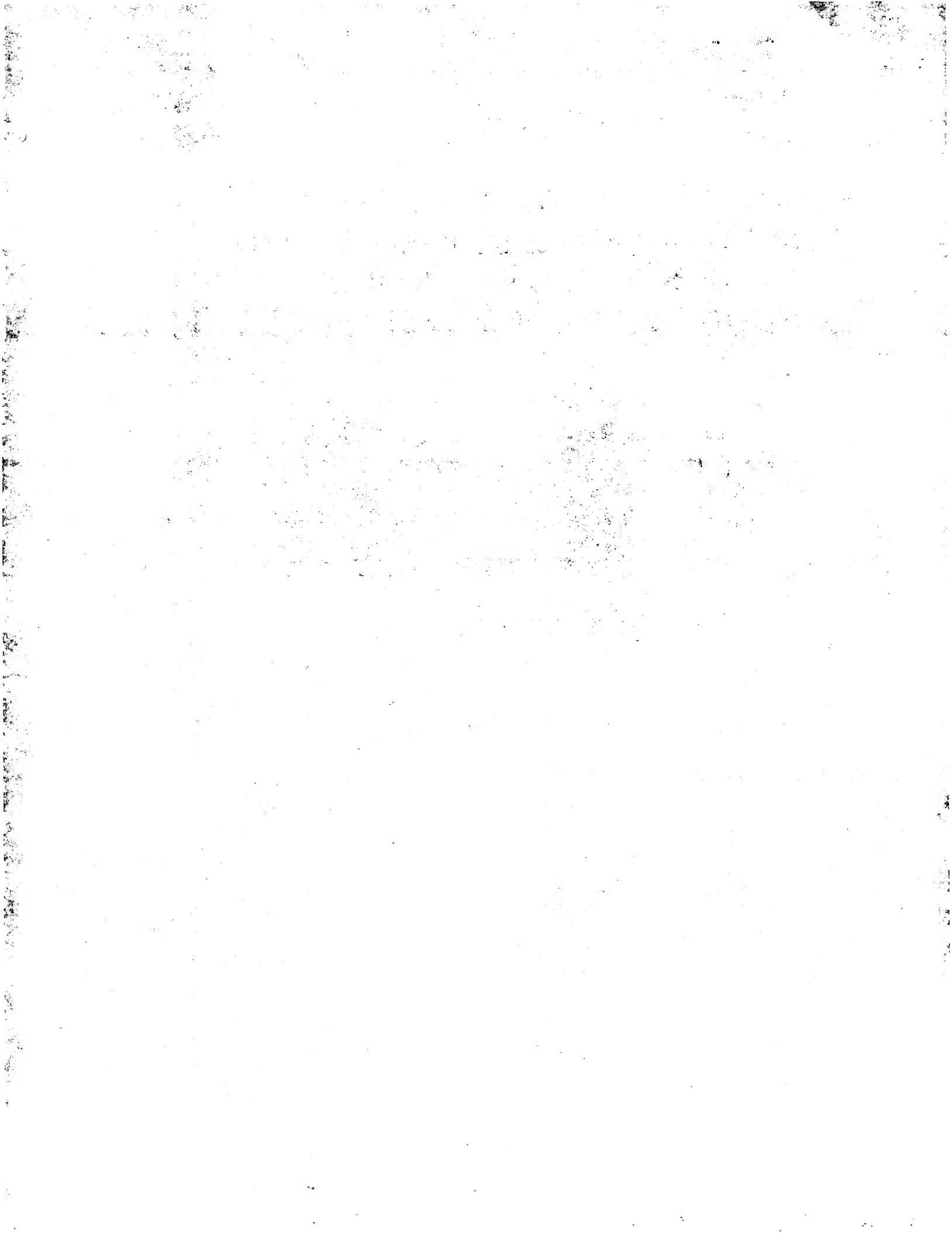


Figure 5. NET CUMULATIVE ENERGY EXPENDITURE WITH LCT AND DESIGNER OIL CONSUMPTION

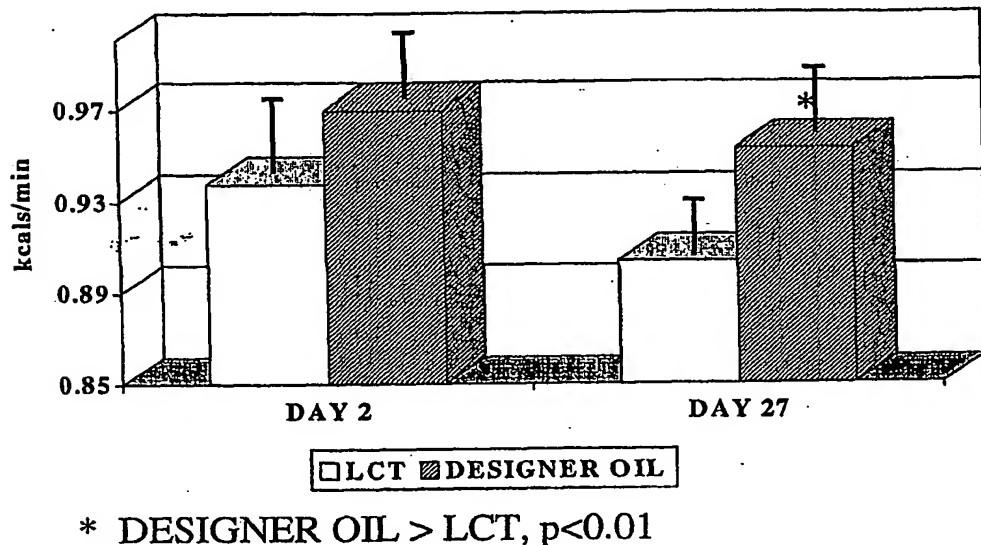
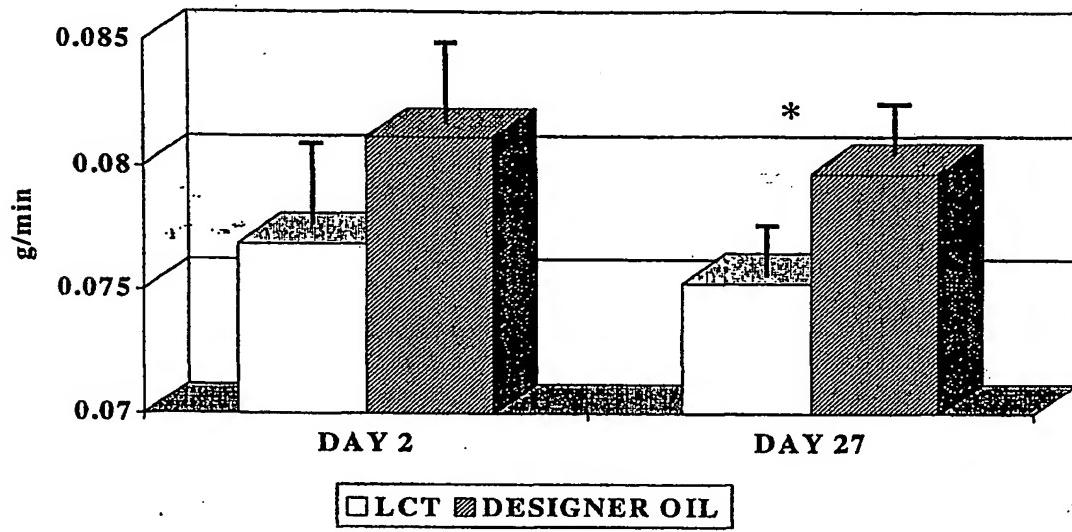


Figure 6. NET CUMULATIVE FAT OXIDATION WITH LCT AND DESIGNER OIL CONSUMPTION



* DESIGNER OIL>LCT, p<0.05

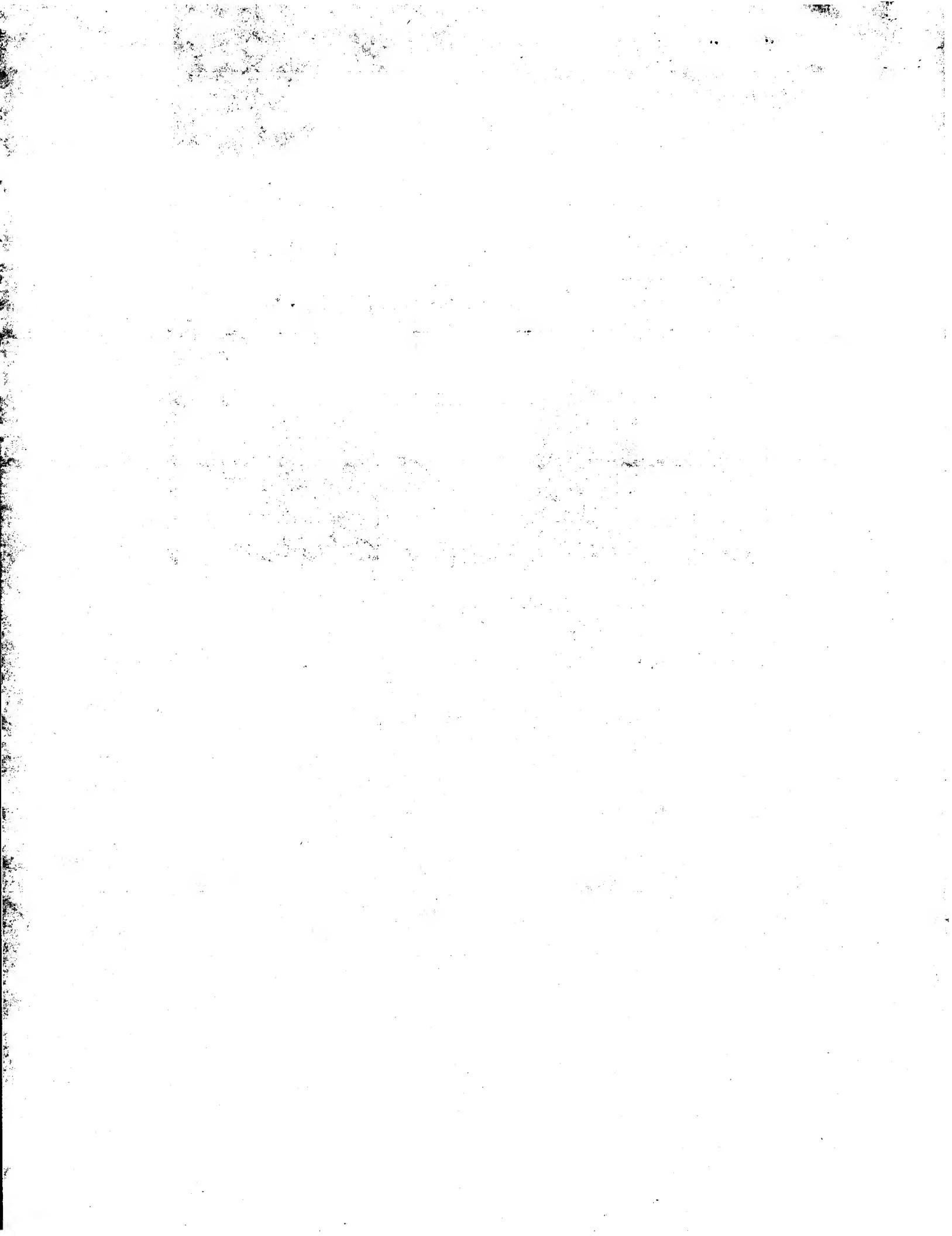
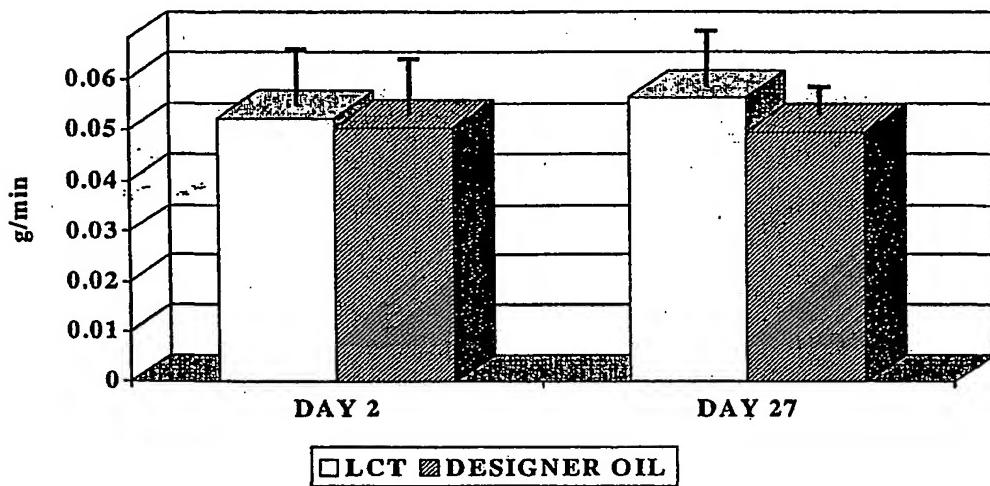


Figure 7. NET CUMULATIVE
CARBOHYDRATE OXIDATION WITH
LCT AND DESIGNER OIL
CONSUMPTION



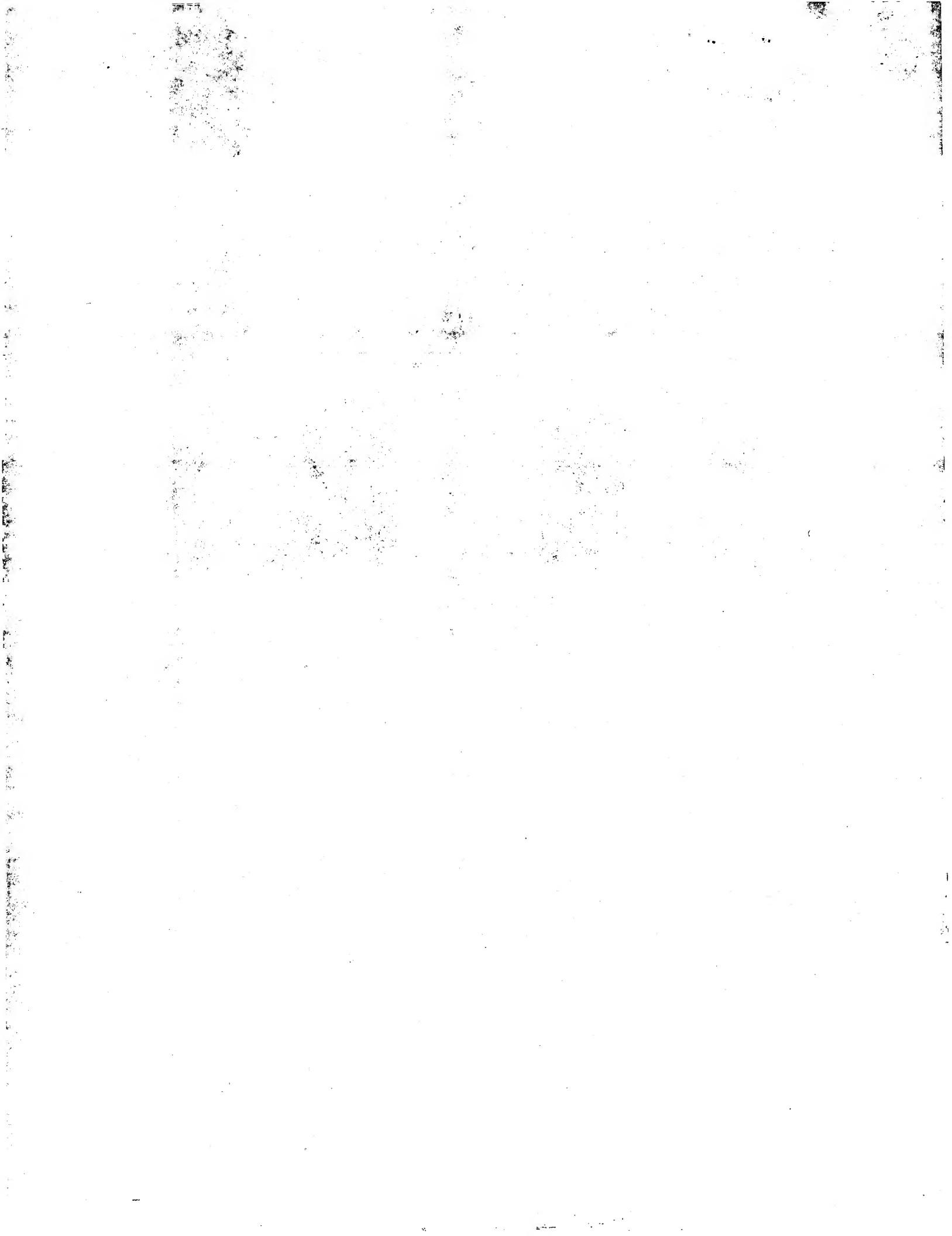
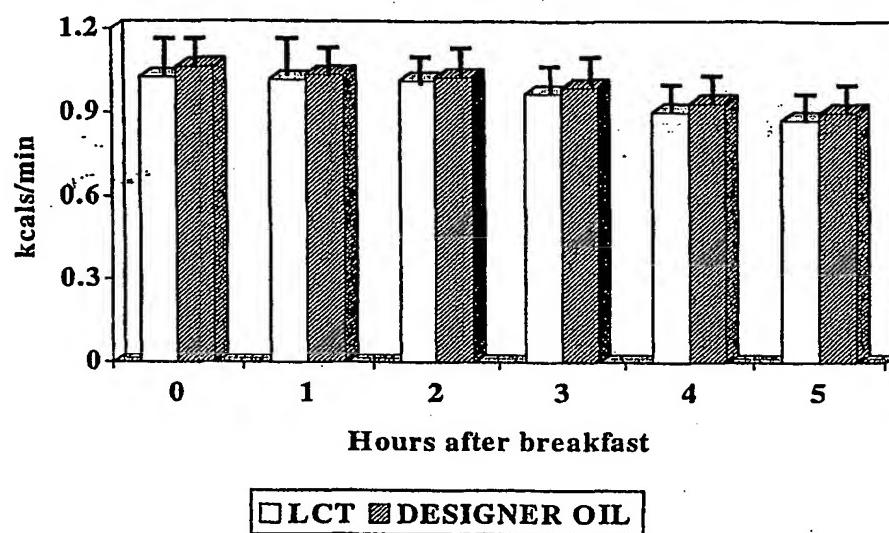


Figure 8. HOURLY ENERGY EXPENDITURE AFTER CONSUMPTION OF A BREAKFAST CONTAINING LCT AND DESIGNER OIL (day2)



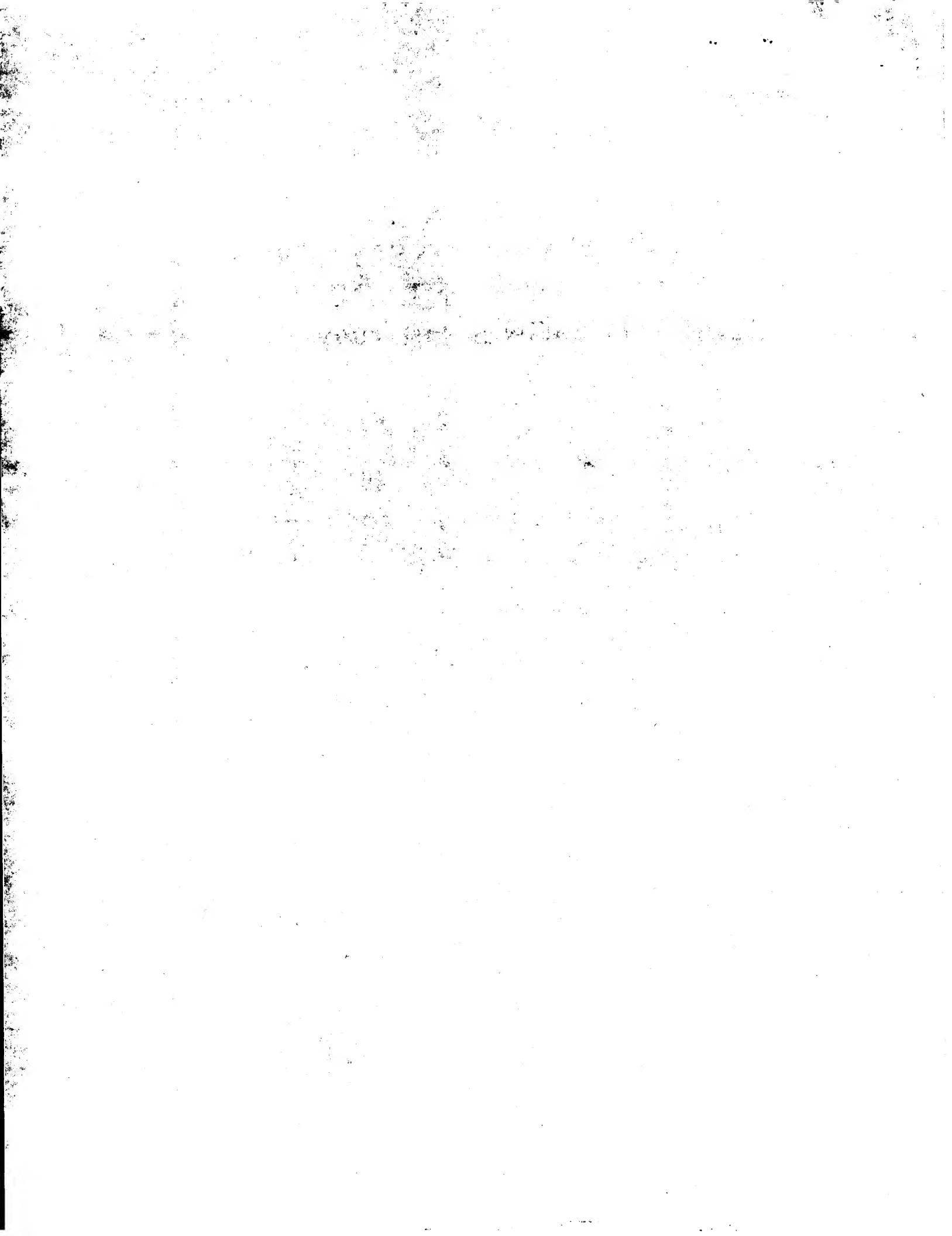
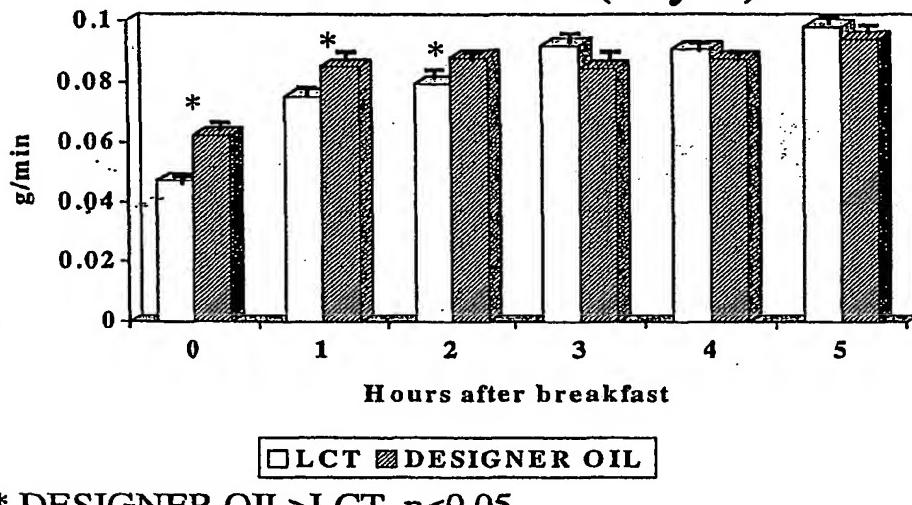


Figure 9. HOURLY FAT OXIDATION
AFTER CONSUMPTION OF A
BREAKFAST CONTAINING LCT AND
DESIGNER OIL (day 2)



* DESIGNER OIL>LCT, p<0.05

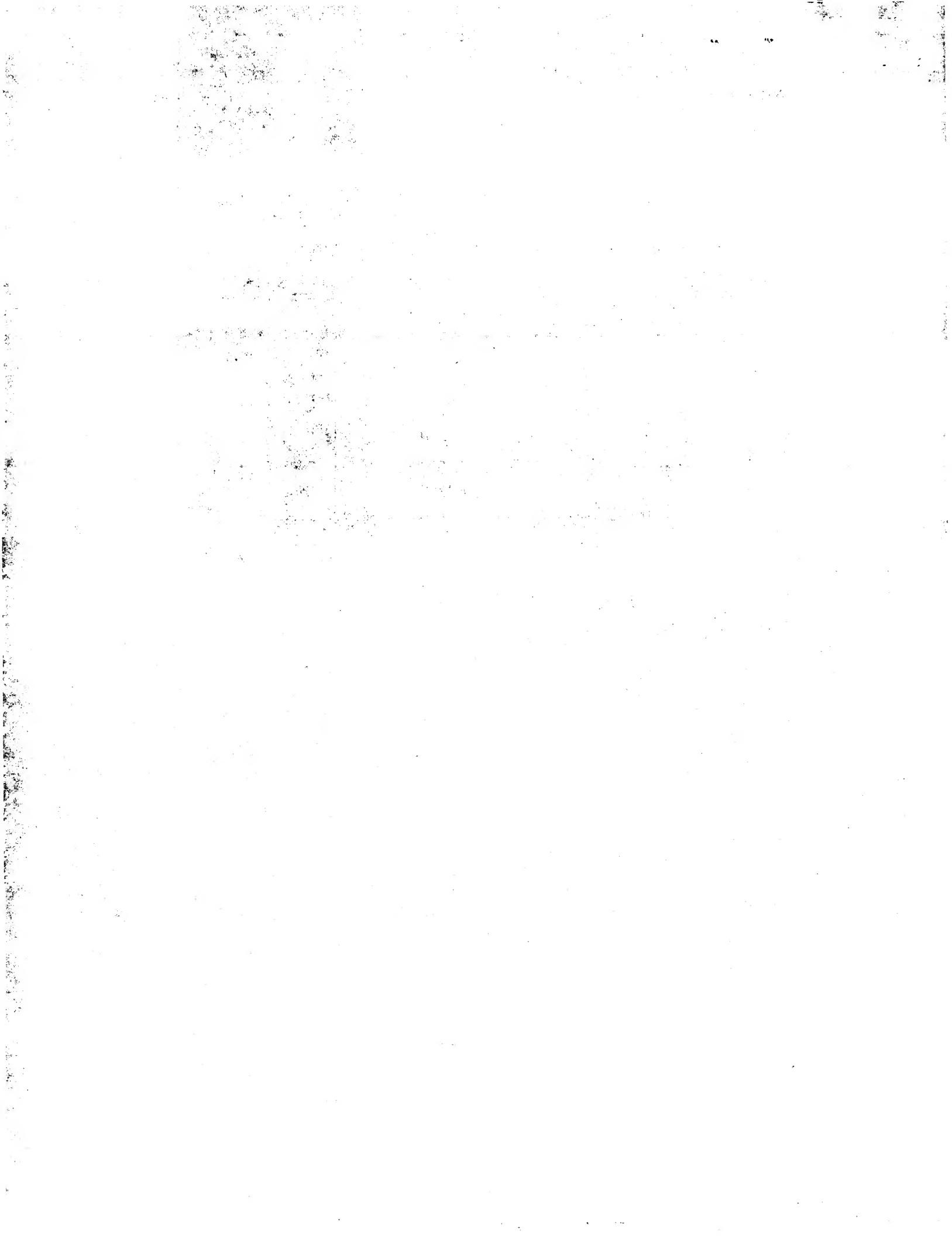
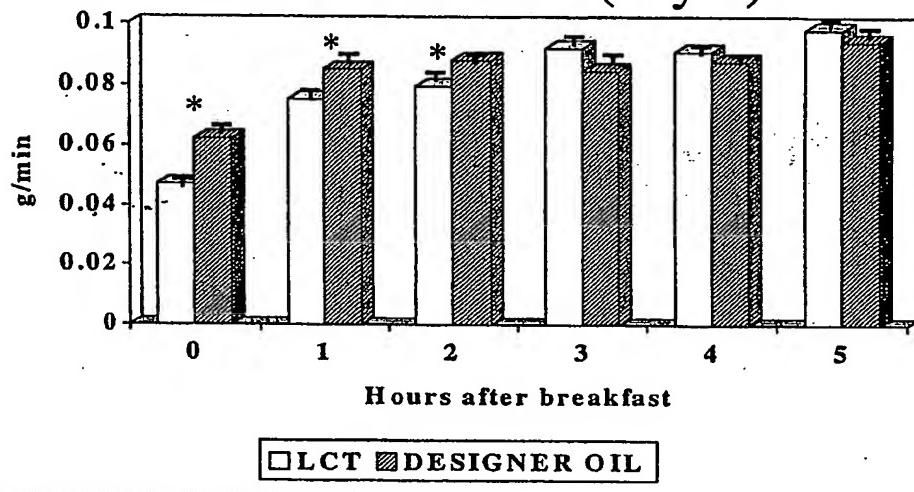


Figure 9. HOURLY FAT OXIDATION
AFTER CONSUMPTION OF A
BREAKFAST CONTAINING LCT AND
DESIGNER OIL (day 2)



* DESIGNER OIL>LCT, p<0.05

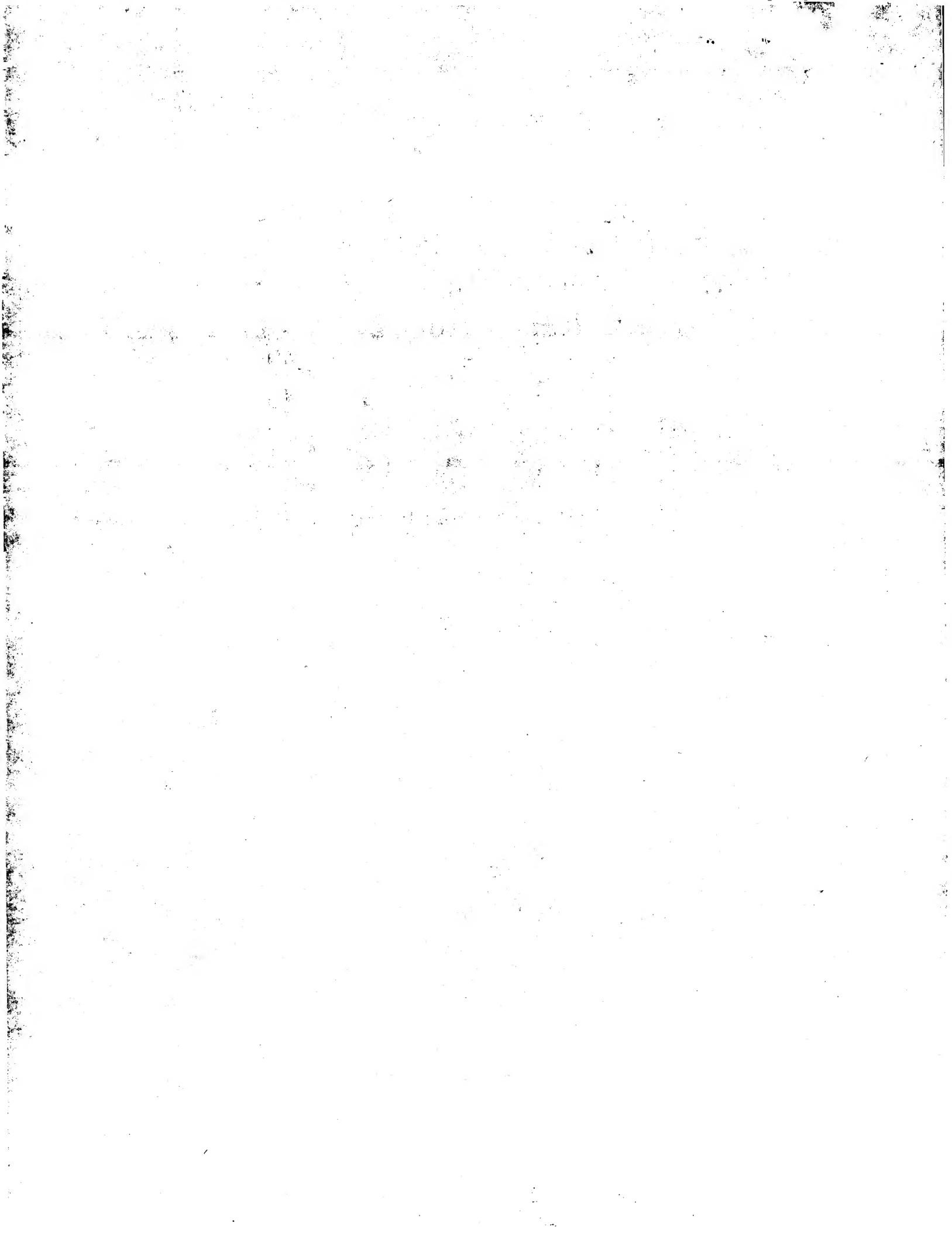
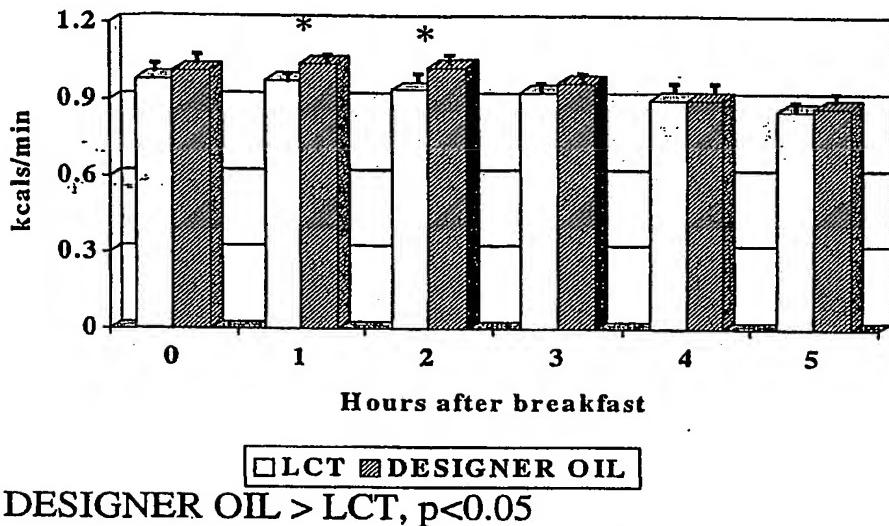


Figure 11. HOURLY ENERGY EXPENDITURE AFTER CONSUMPTION OF A BREAKFAST CONTAINING LCT AND DESIGNER OIL (day 27)



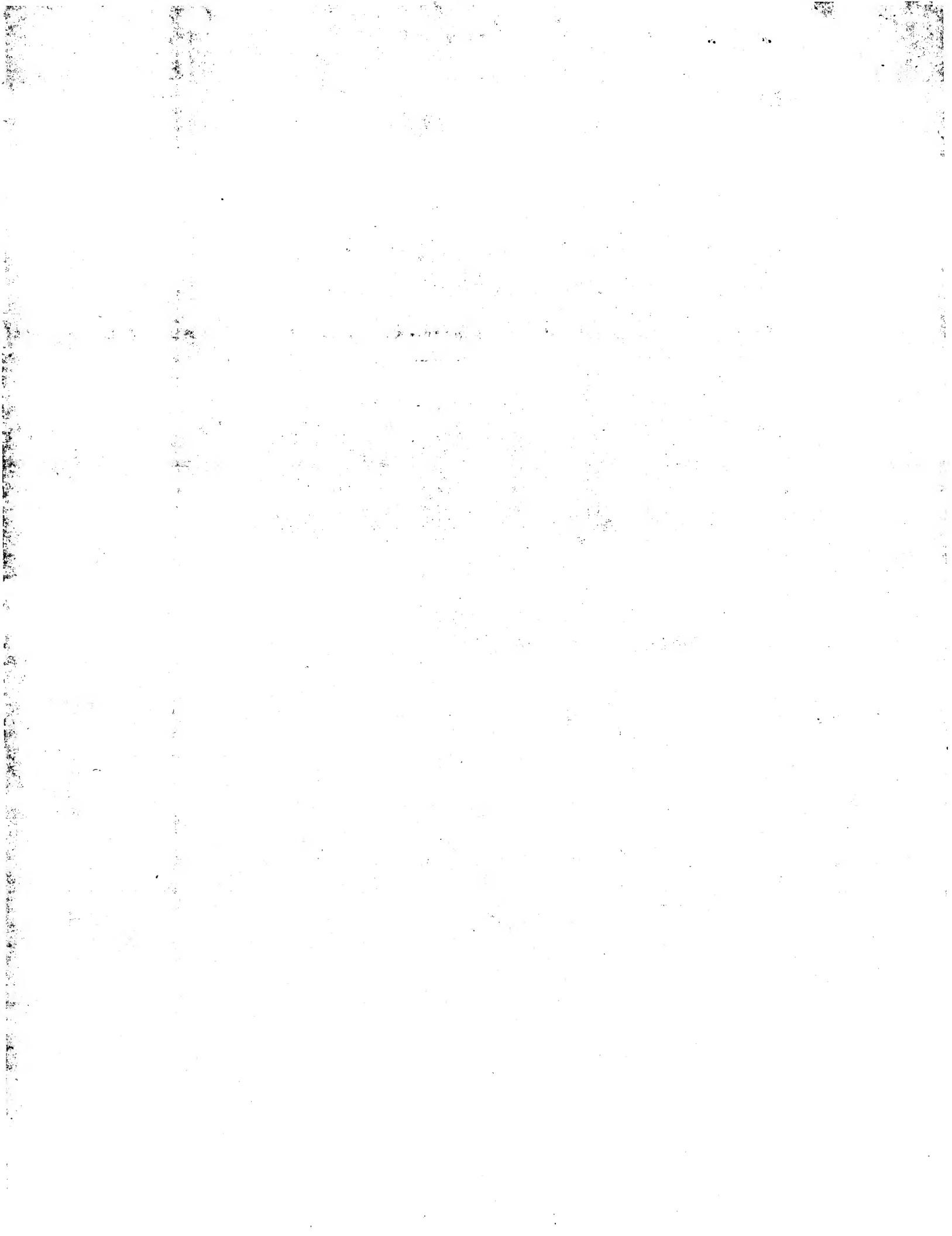
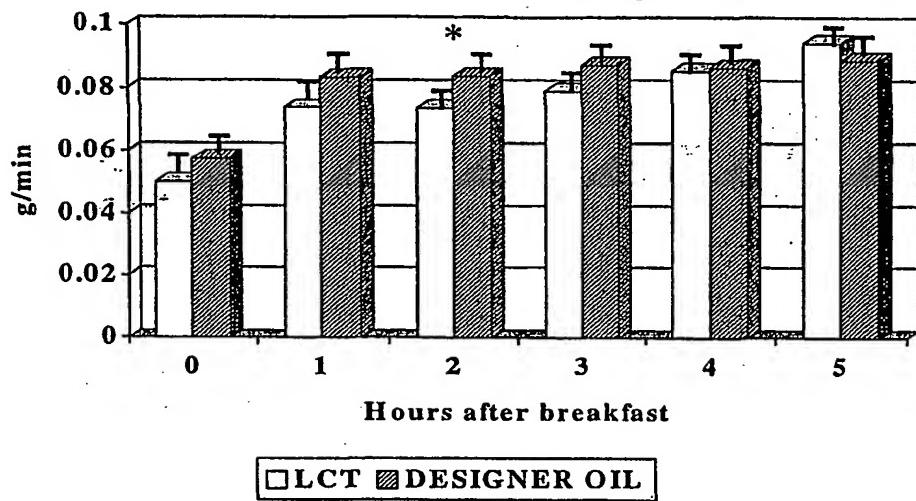


Figure 12. HOURLY FAT OXIDATION
AFTER CONSUMPTION OF A
BREAKFAST CONTAINING LCT AND
DESIGNER OIL (day 27)



* DESIGNER OIL>LCT, p<0.05

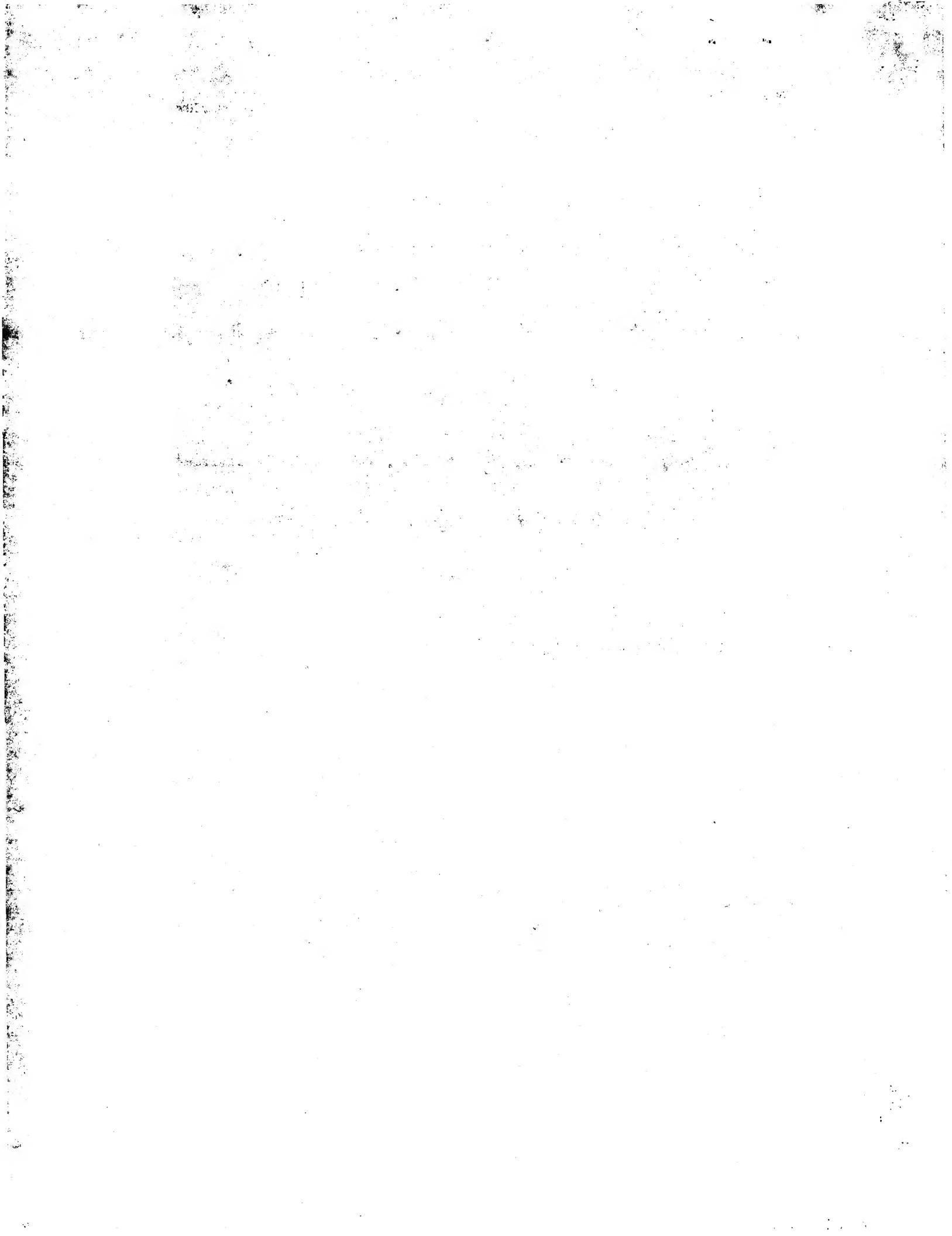
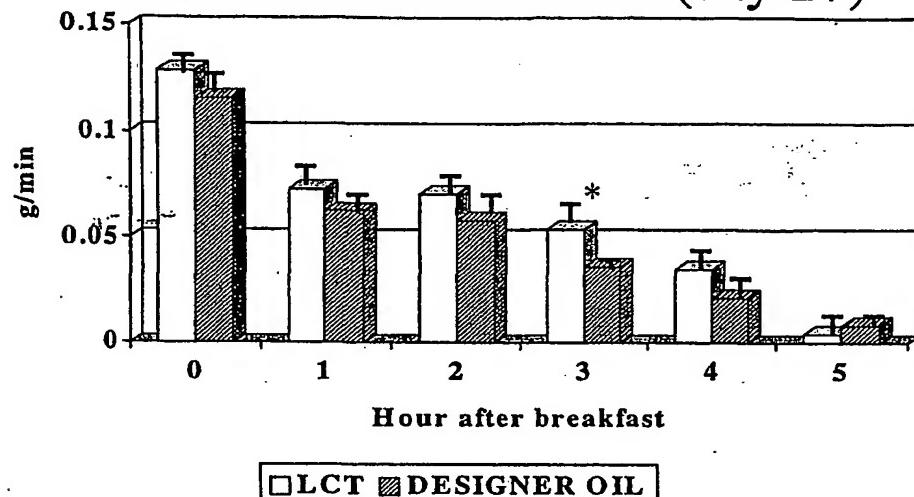


Figure 13. HOURLY CARBOHYDRATE OXIDATION AFTER CONSUMPTION OF A BREAKFAST CONTAINING LCT AND DESIGNER OIL (day 27)



* LCT > DESIGNER OIL, p<0.05

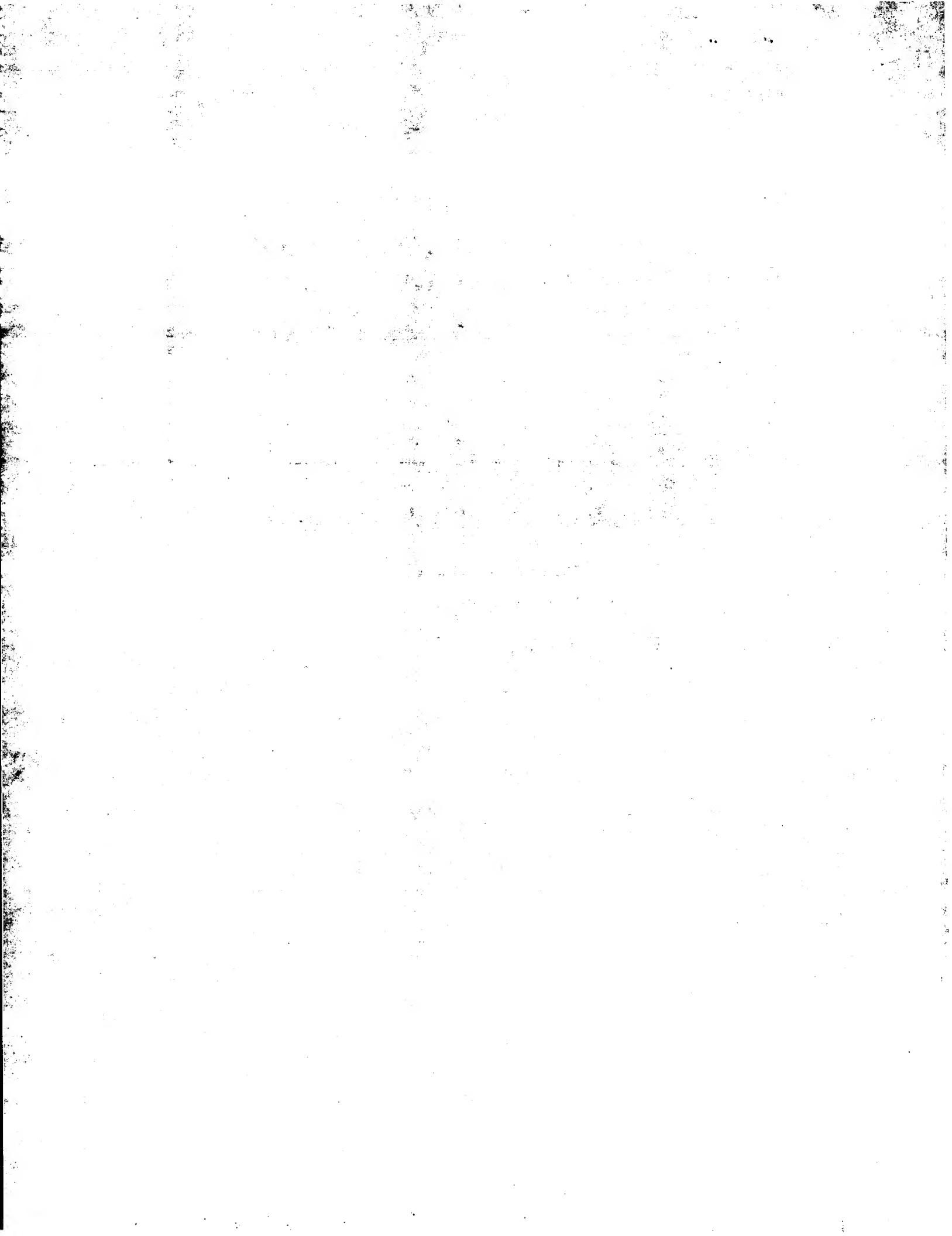
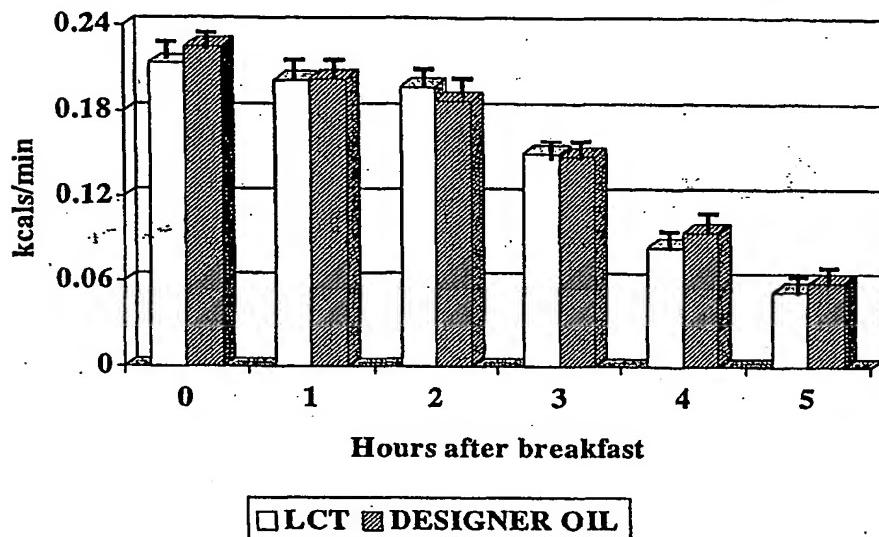


Figure 14. THERMIC EFFECT OF A
BREAKFAST CONTAINING
LCT AND DESIGNER OIL (day2)



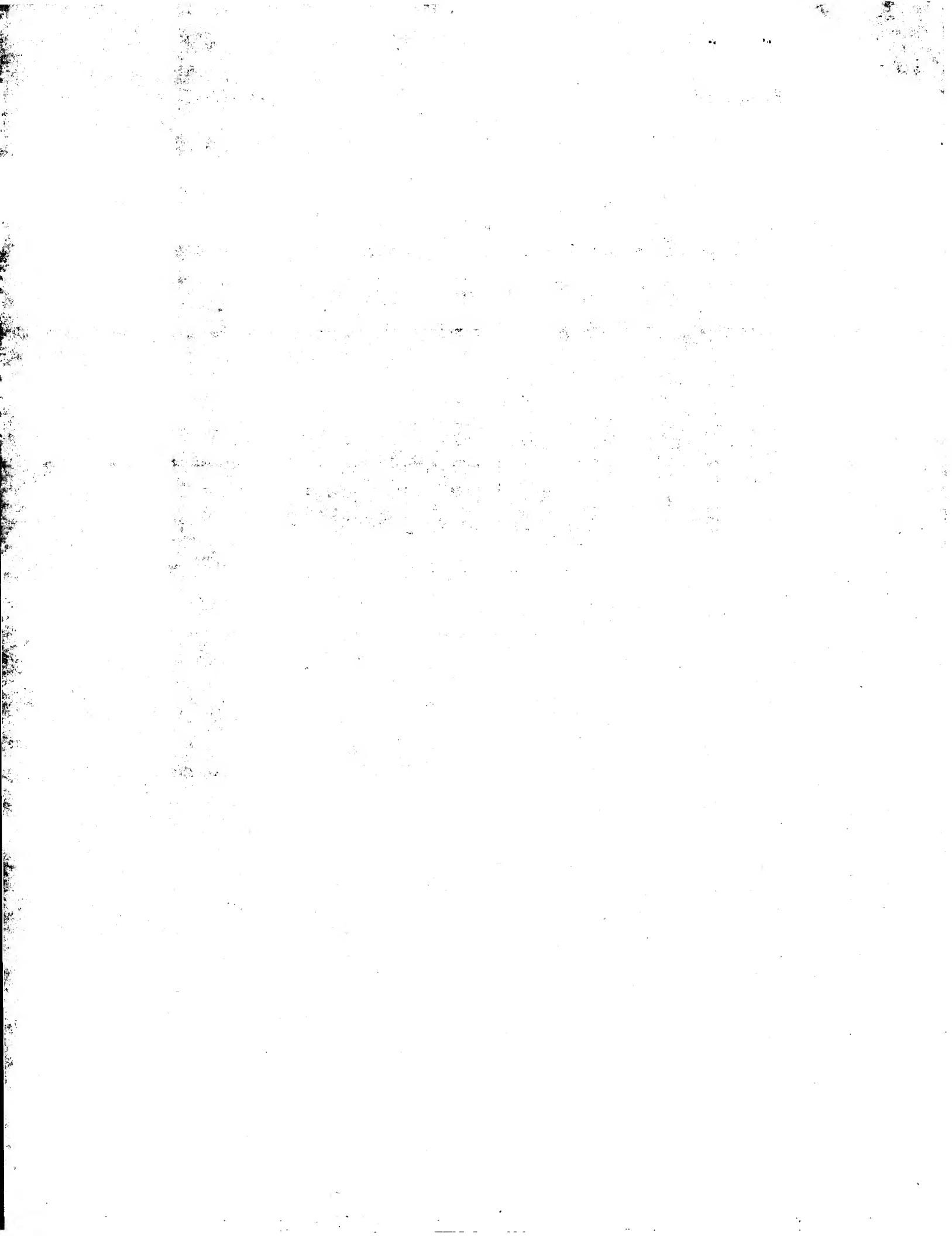
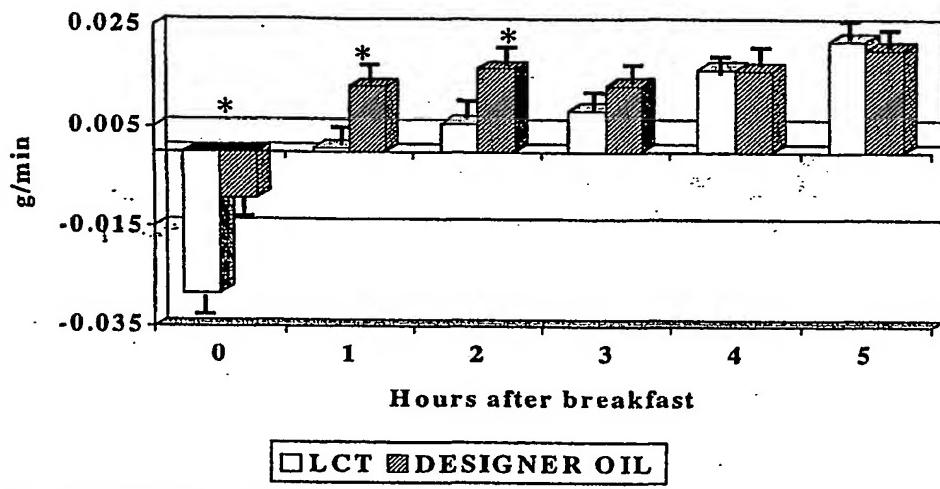


Figure 15. THERMIC EFFECT OF FOOD:
FAT OXIDATION AFTER CONSUMPTION OF
A BREAKFAST CONTAINING
LCT AND DESIGNER OIL (day 2)



* DESIGNER OIL > LCT, p<0.05

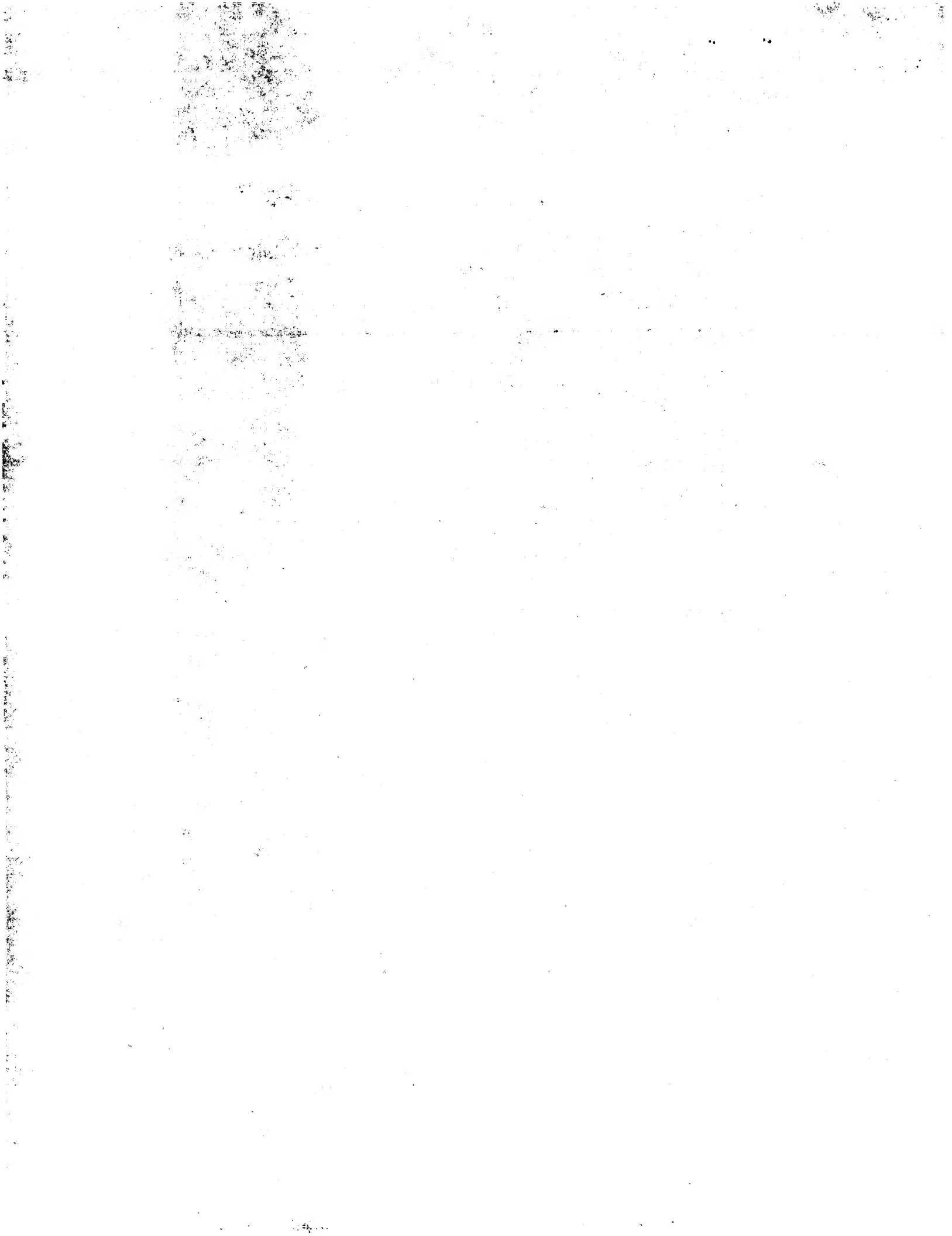
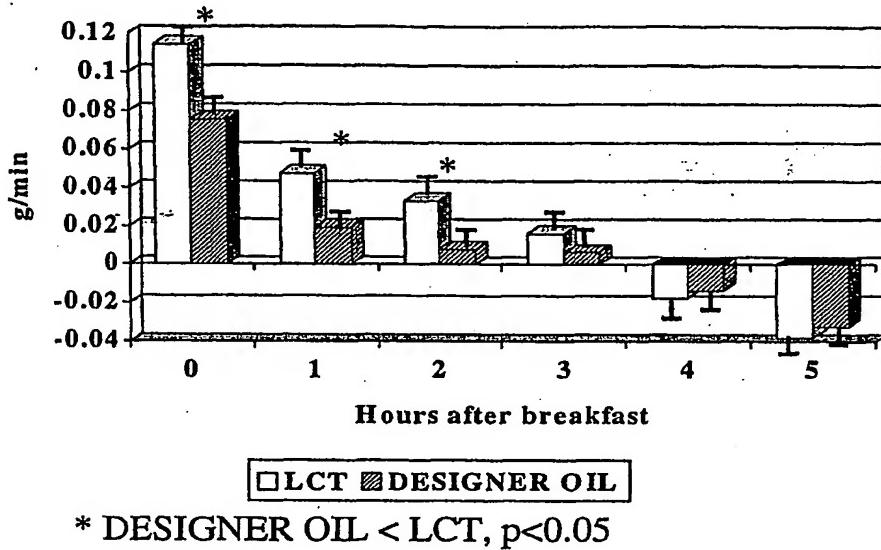


Figure 16. THERMIC EFFECT OF FOOD:
CARBOHYDRATE OXIDATION AFTER
CONSUMPTION OF A BREAKFAST
CONTAINING LCT AND DESIGNER OIL (day 2)



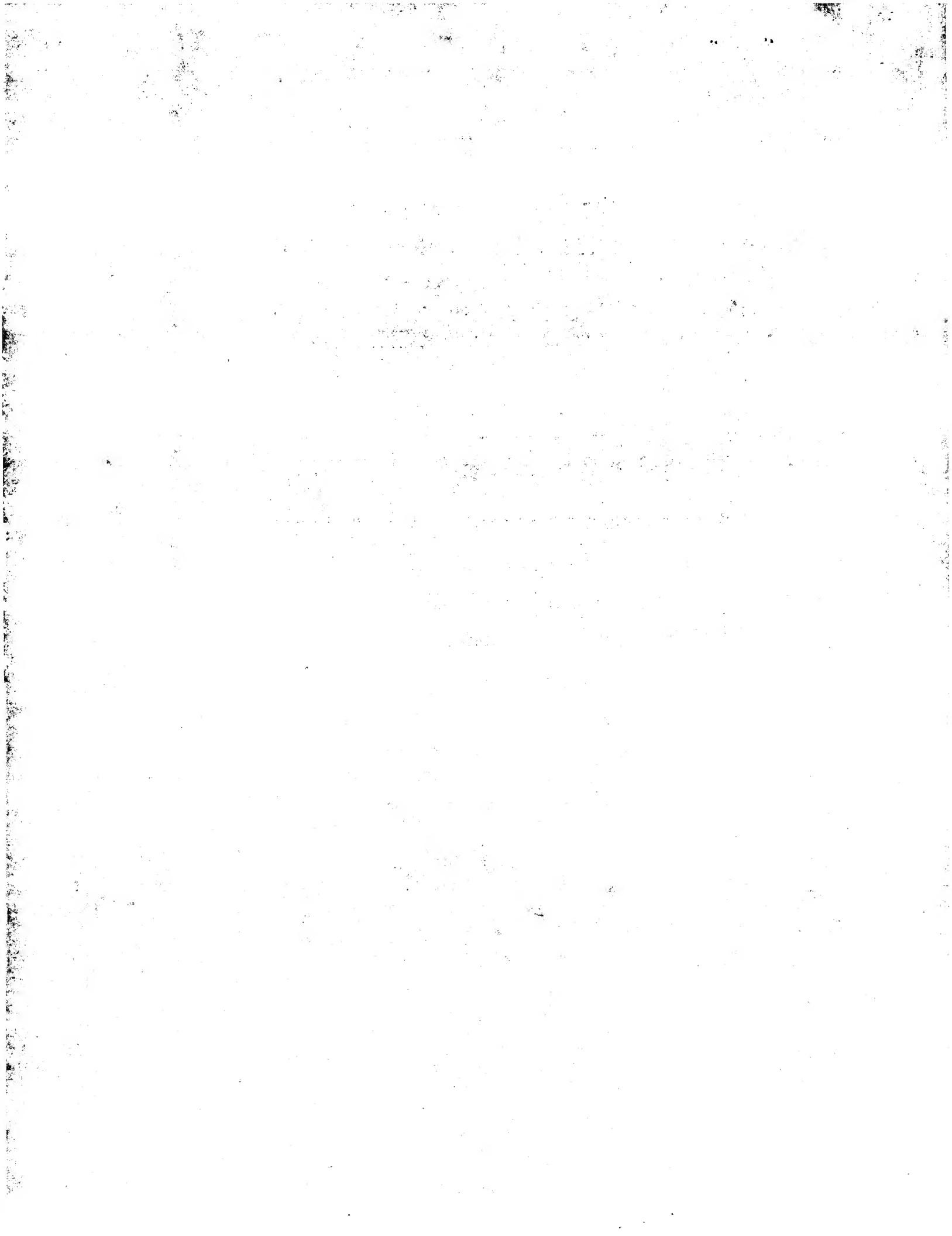
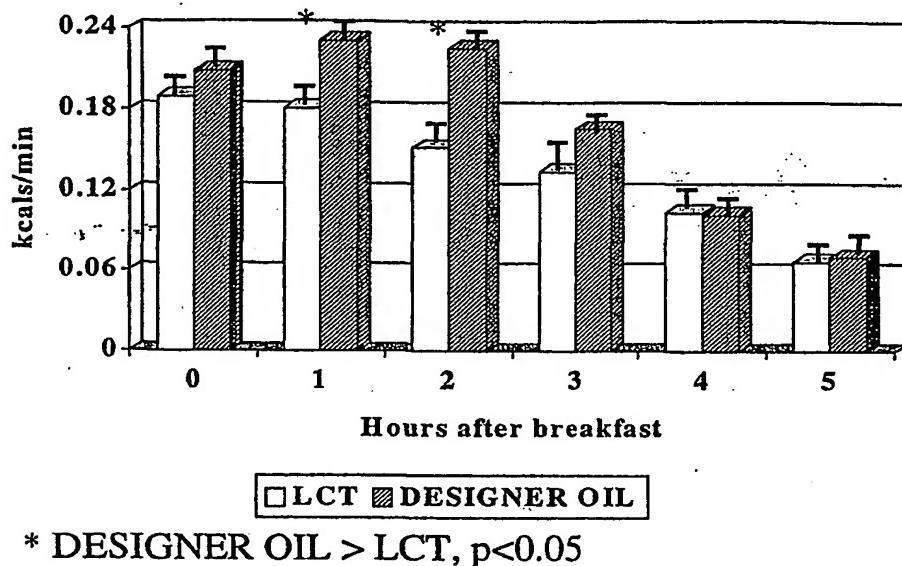


Figure 17. THERMIC EFFECT OF A BREAKFAST CONTAINING LCT AND DESIGNER OIL (day 27)



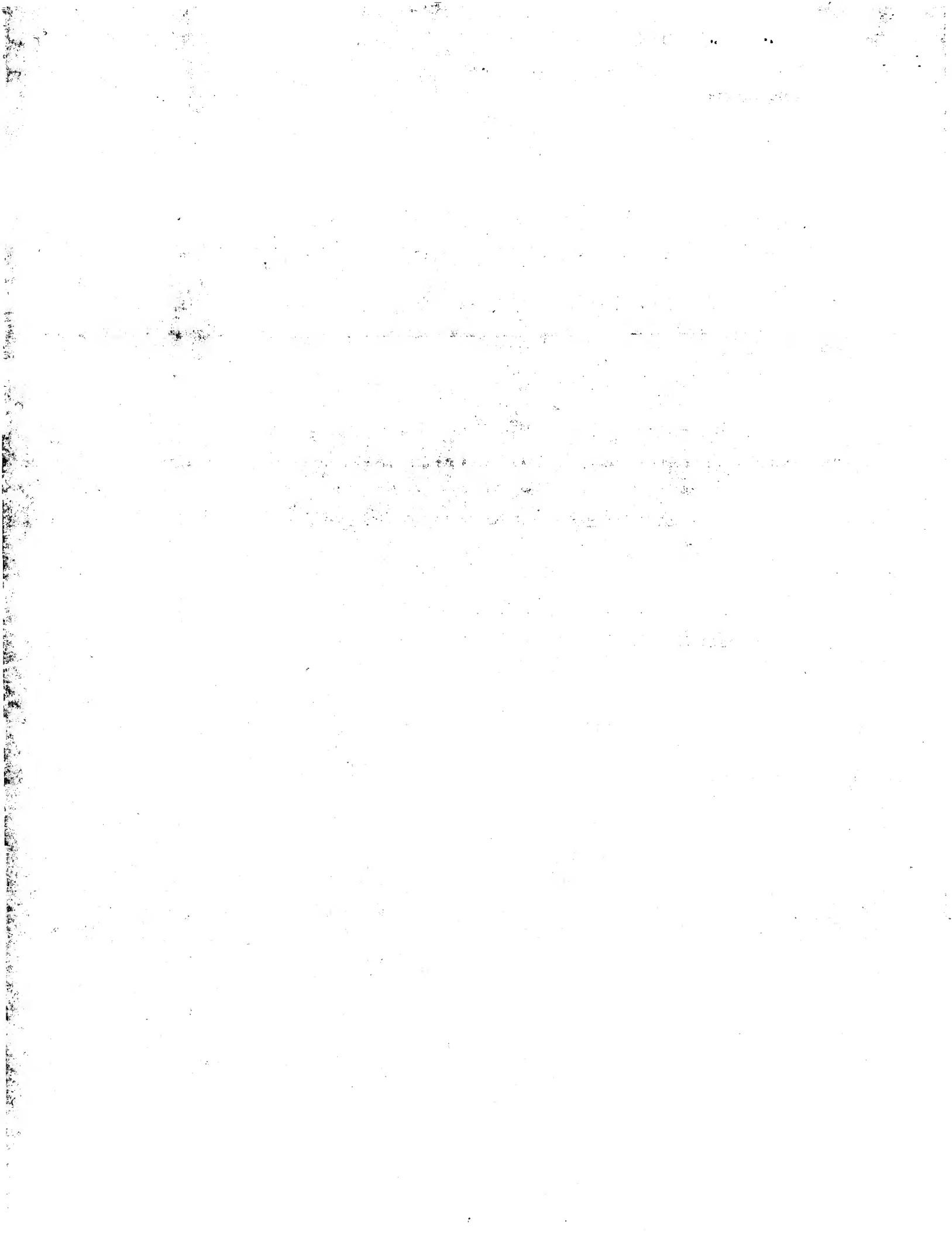
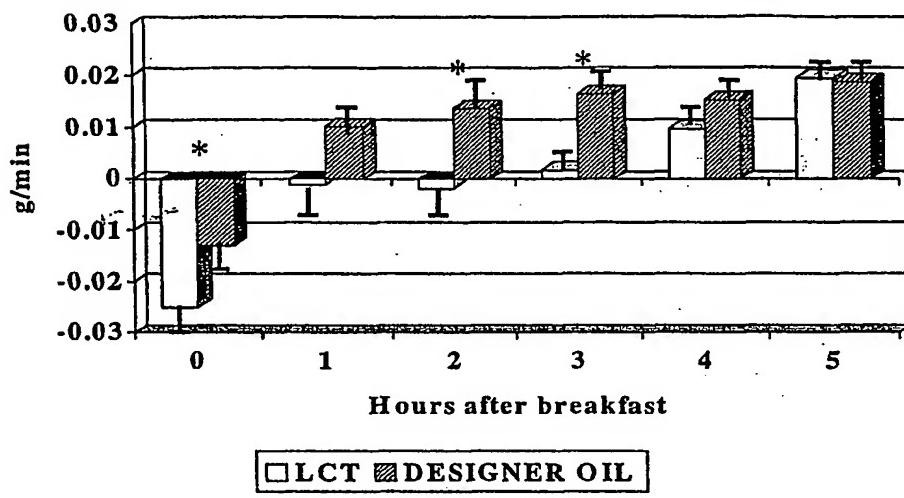


Figure 18. THERMIC EFFECT OF FOOD:
FAT OXIDATION AFTER CONSUMPTION OF
A BREAKFAST CONTAINING
LCT AND DESIGNER OIL (day 27)



* DESIGNER OIL > LCT, p<0.05

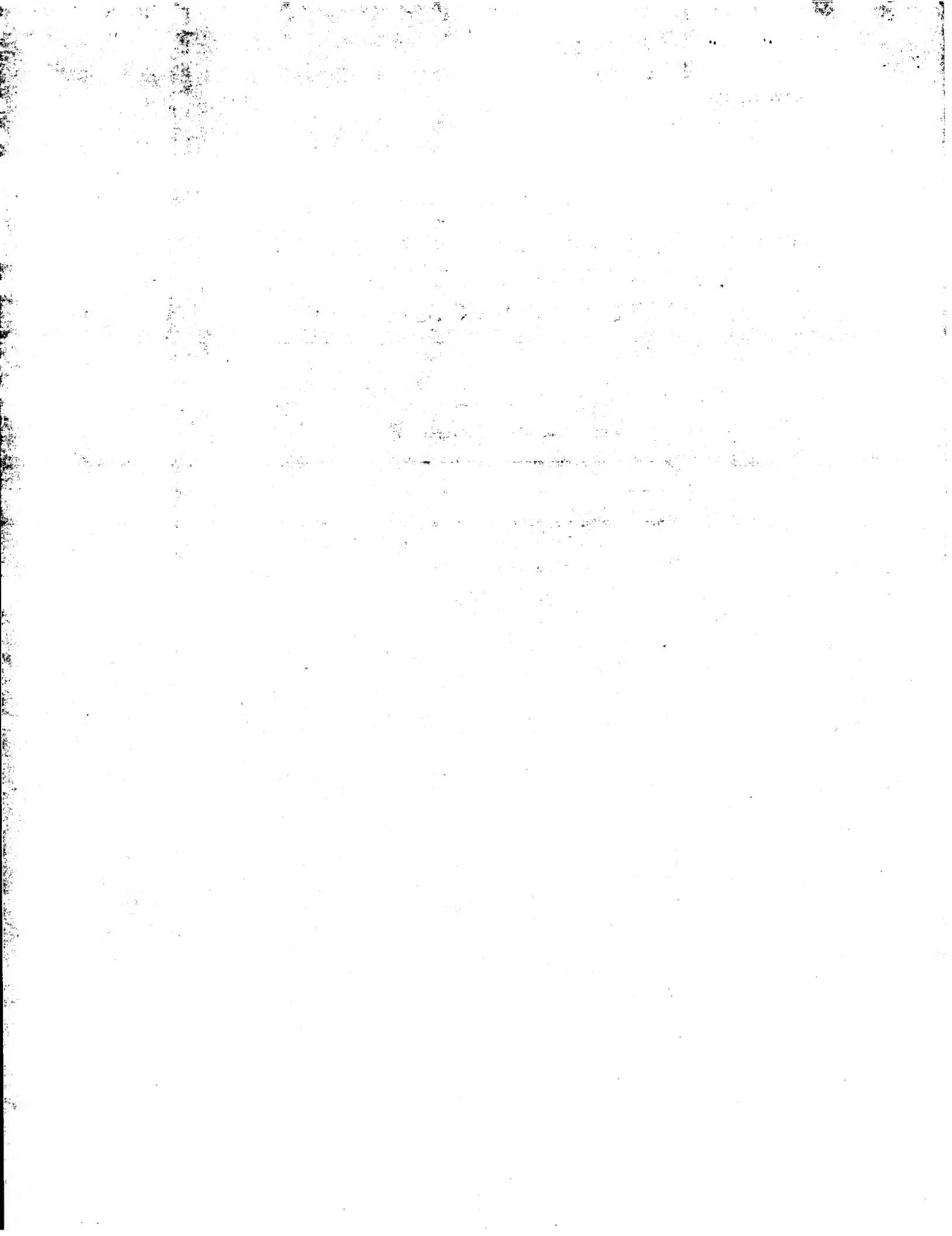
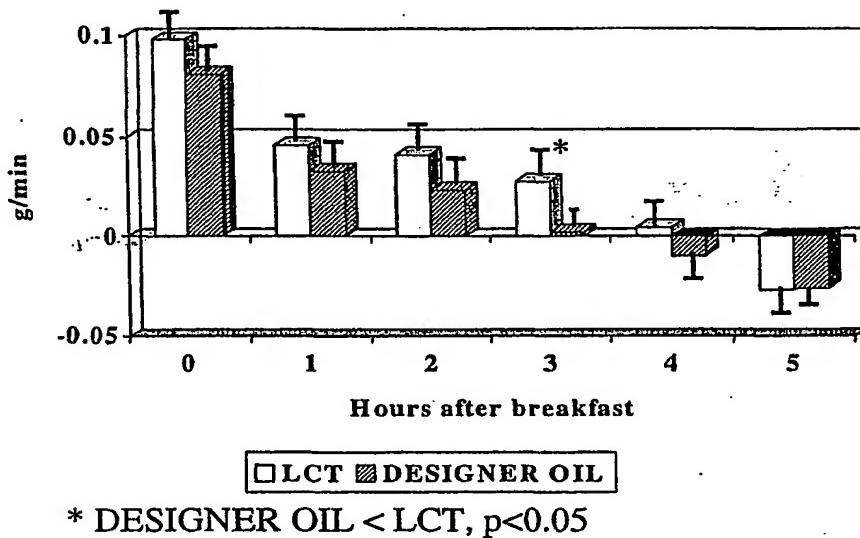


Figure 19. THERMIC EFFECT OF FOOD:
CARBOHYDRATE OXIDATION AFTER
CONSUMPTION OF A BREAKFAST
CONTAINING LCT AND DESIGNER OIL (day 27)



* DESIGNER OIL < LCT, p<0.05

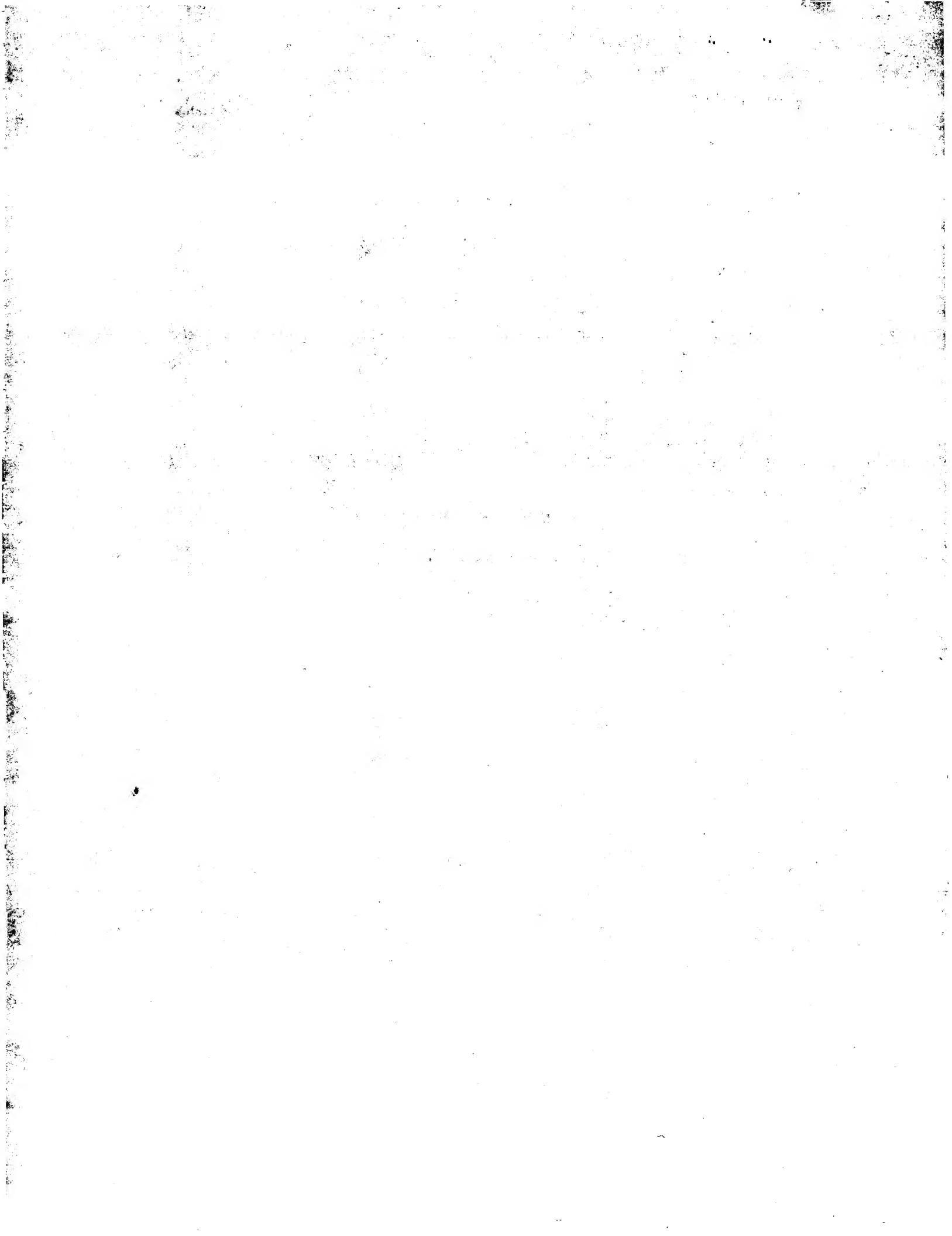
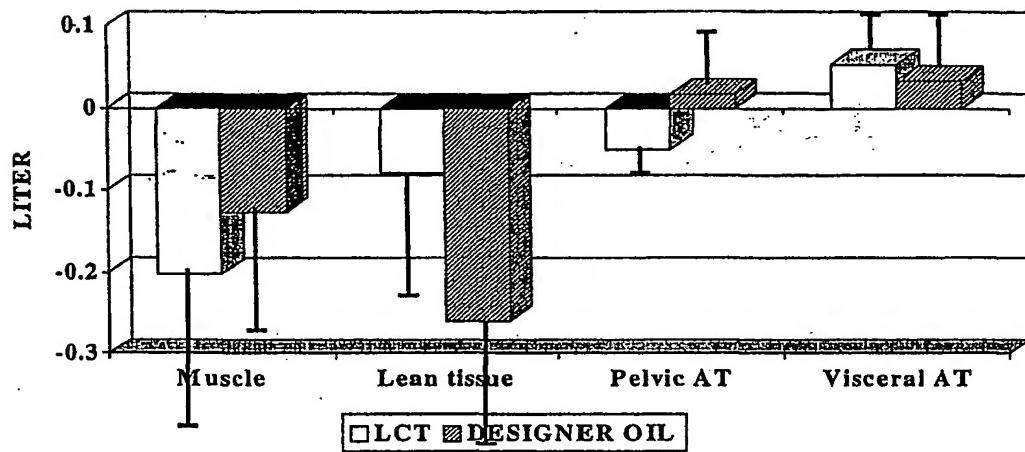


Figure 20. CHANGE IN VOLUME OF
BODY COMPARTMENTS AFTER
28 DAYS OF LCT AND
DESIGNER OIL FEEDING



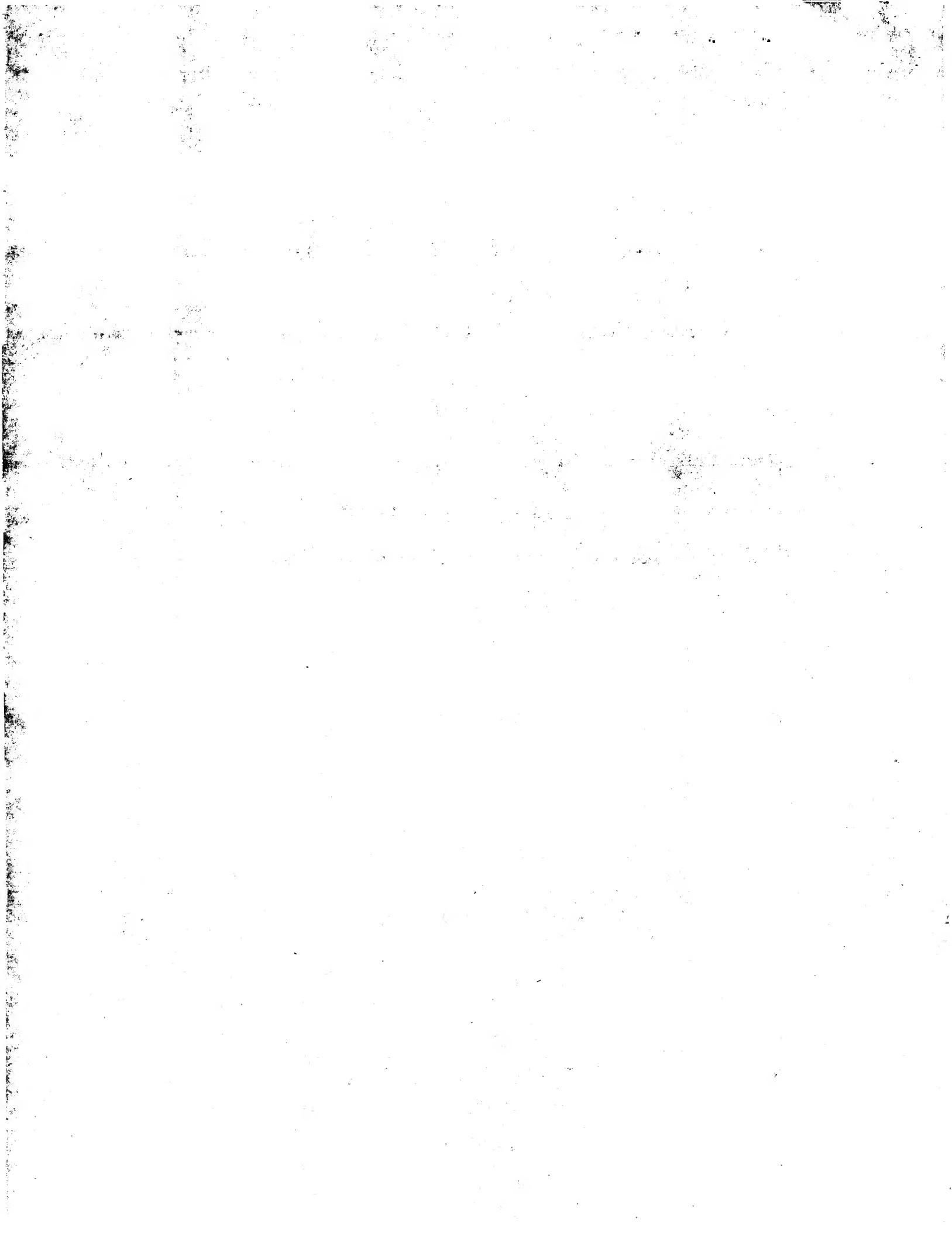
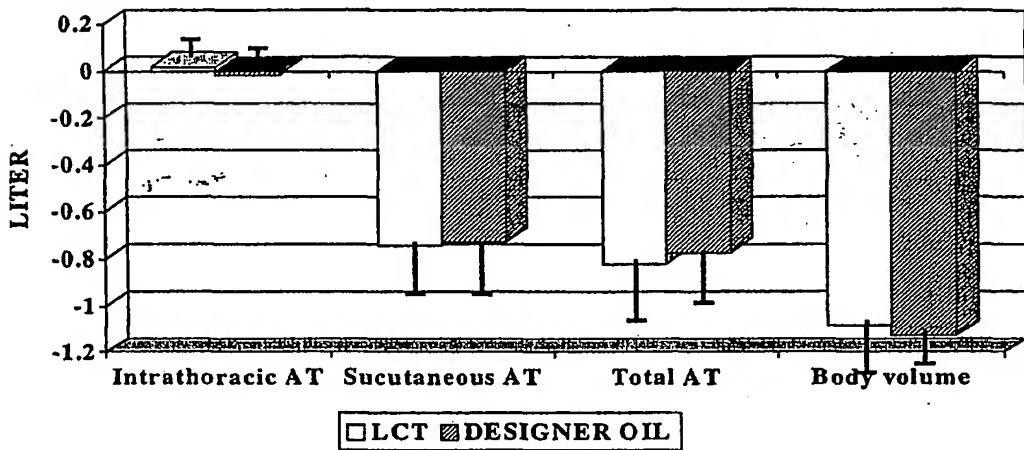


Figure 21. CHANGE IN VOLUME OF
BODY COMPARTMENTS AFTER
28 DAYS OF LCT AND
DESIGNER OIL FEEDING



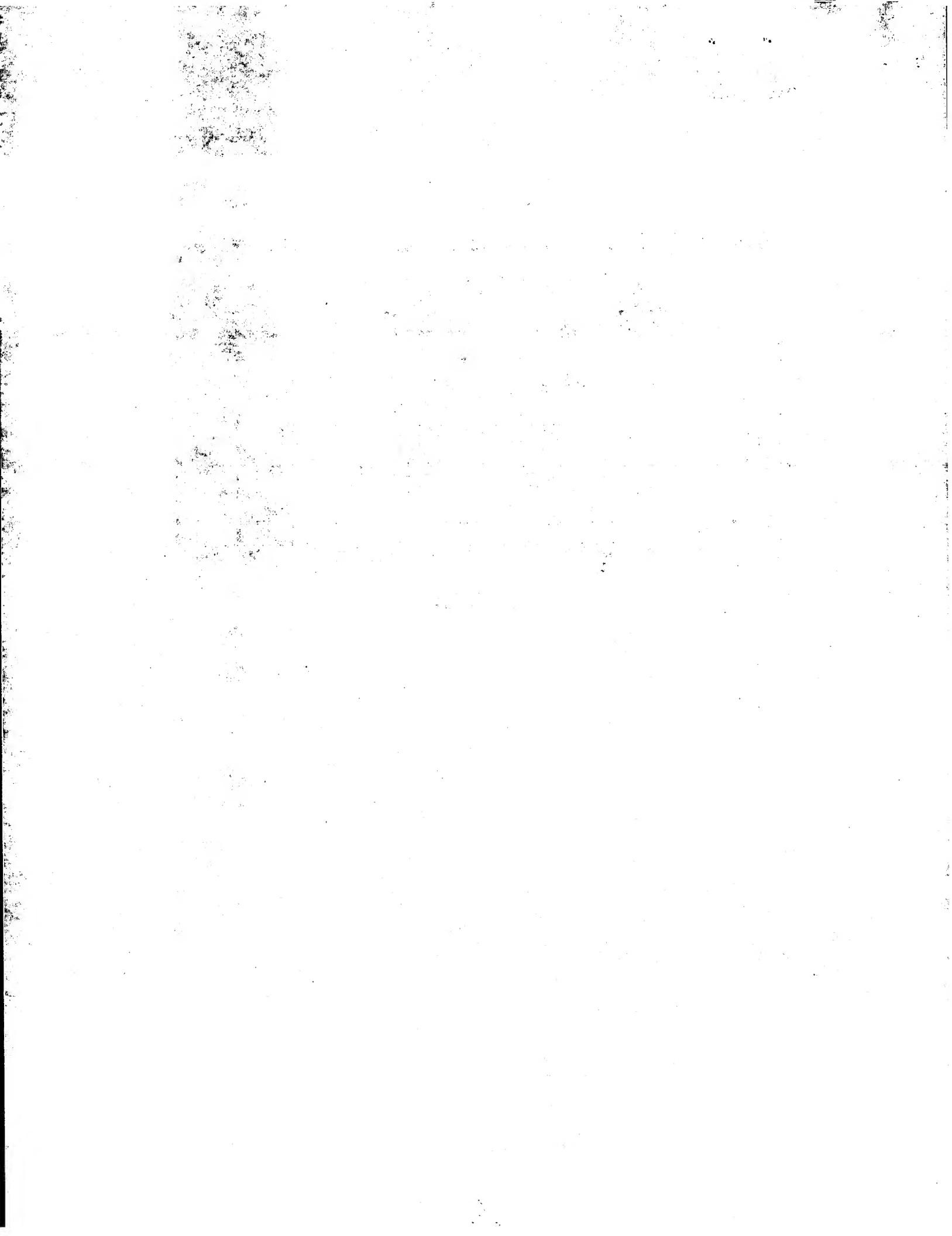
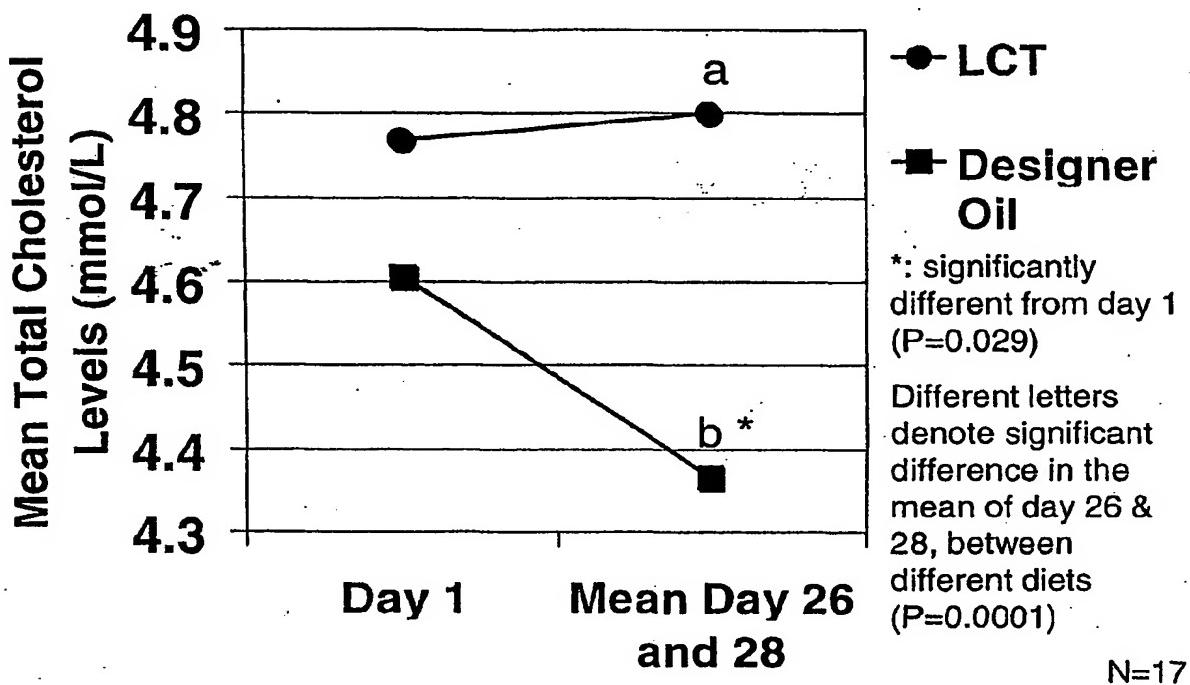


Figure 22: Total Cholesterol Absolute Levels After 28 Days of LCT and Designer Oil Feeding



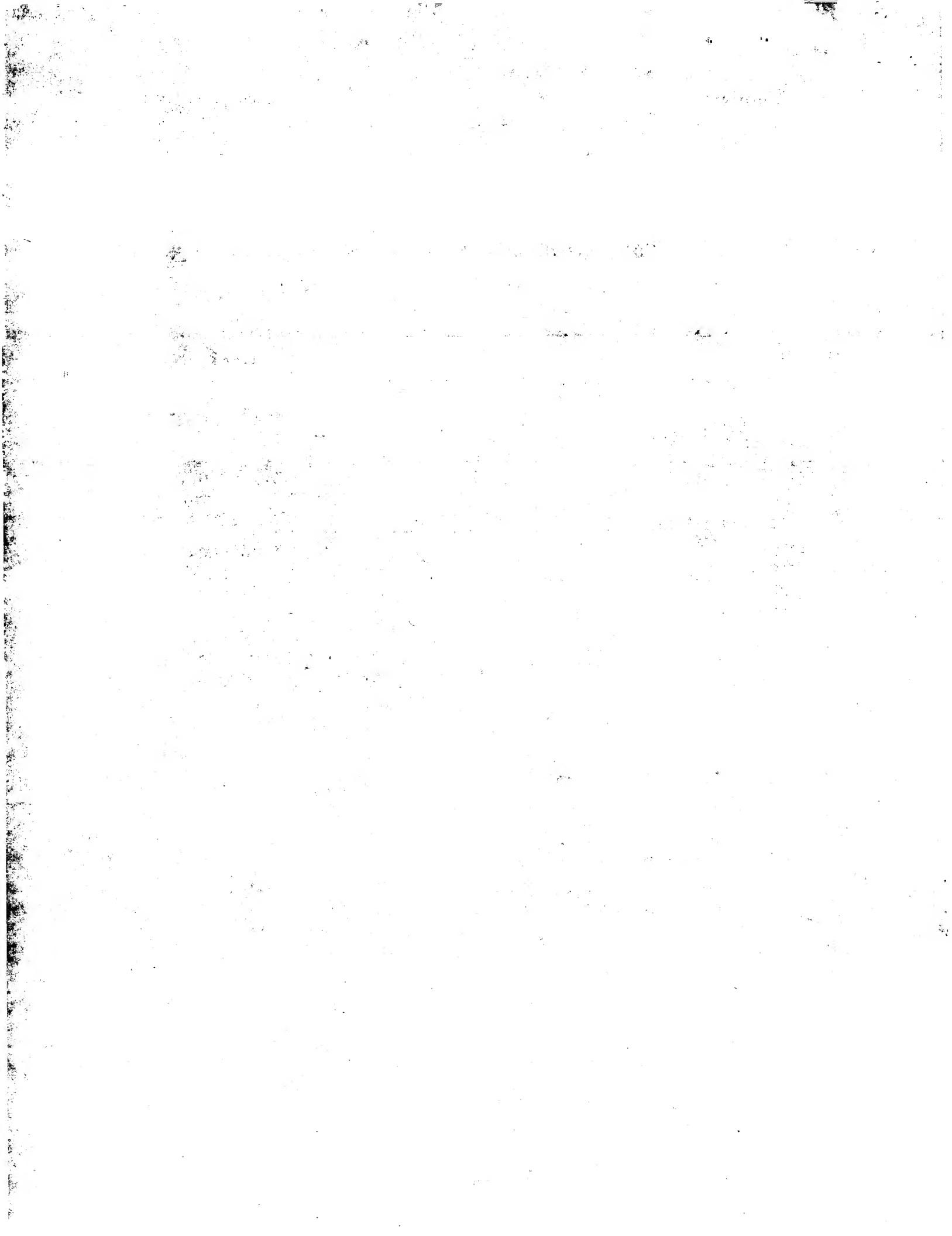
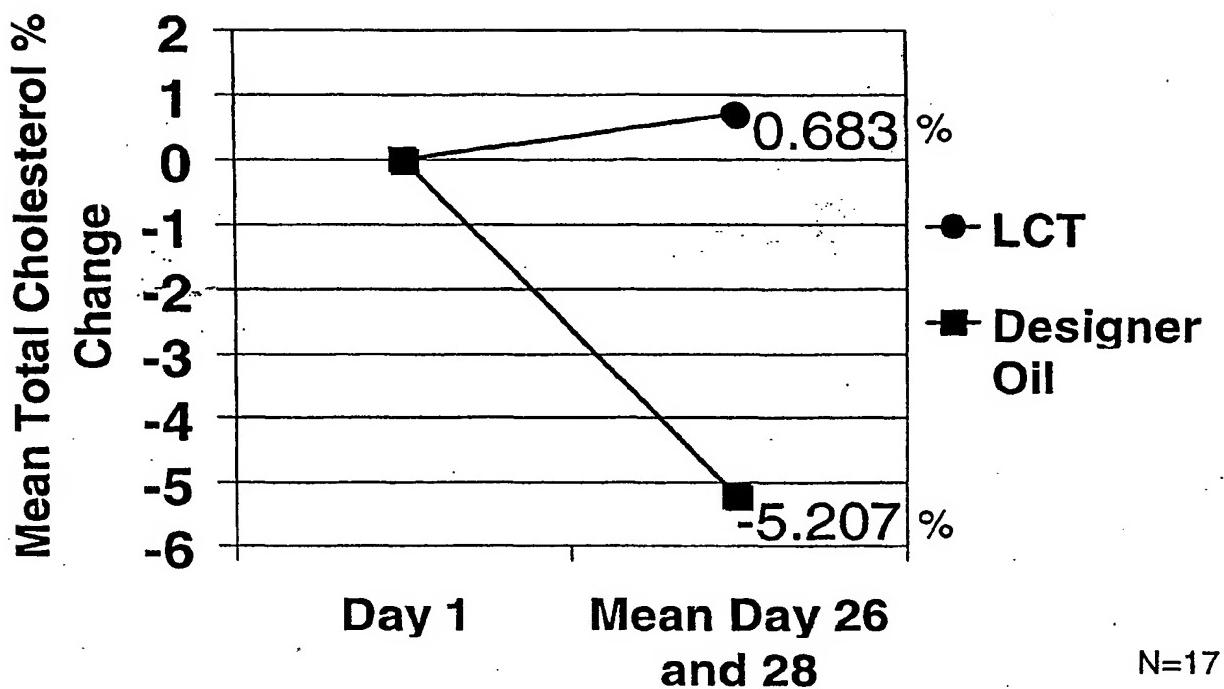


Figure 23: Total Cholesterol Percentage Change After 28 Days of LCT and Designer Oil Feeding



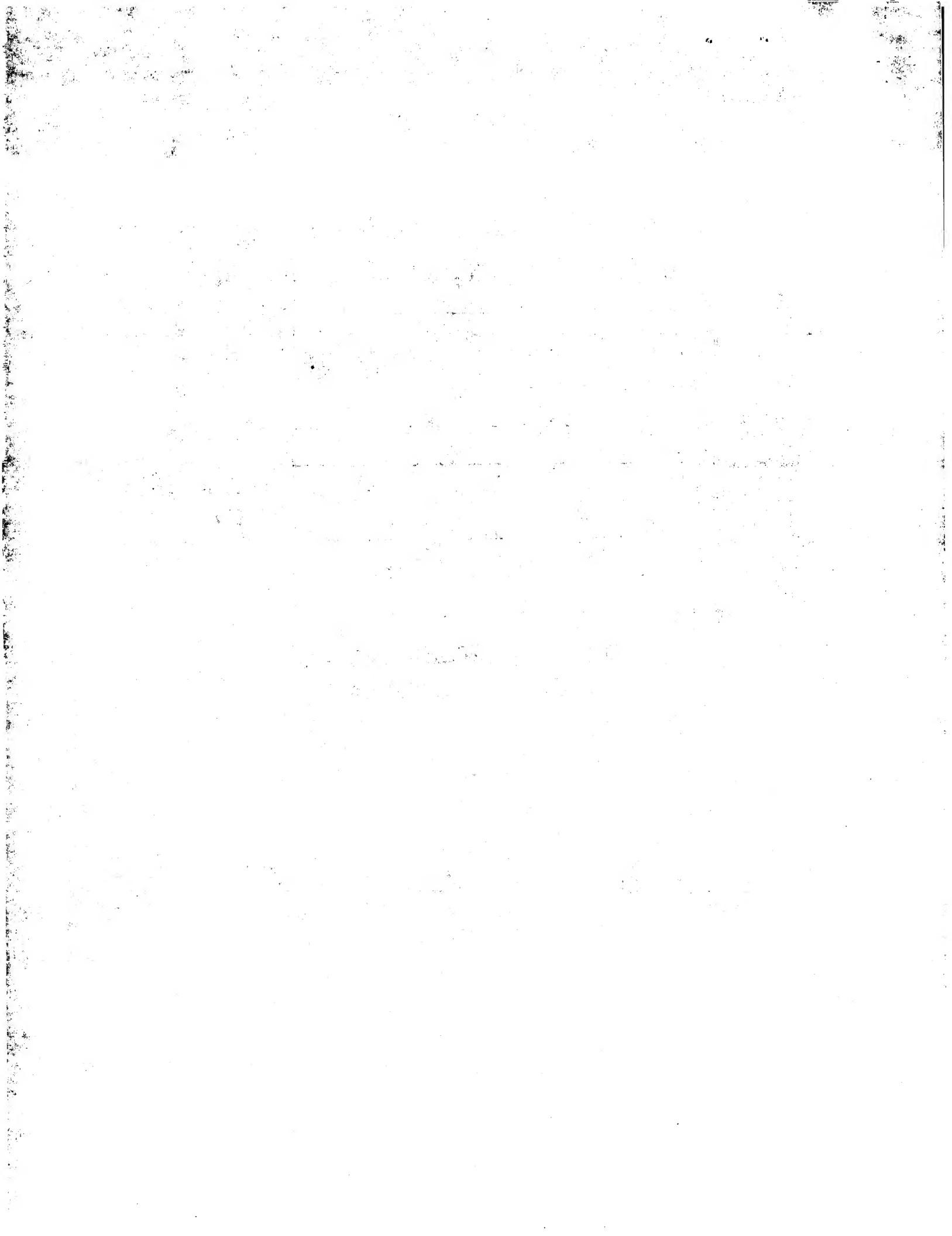
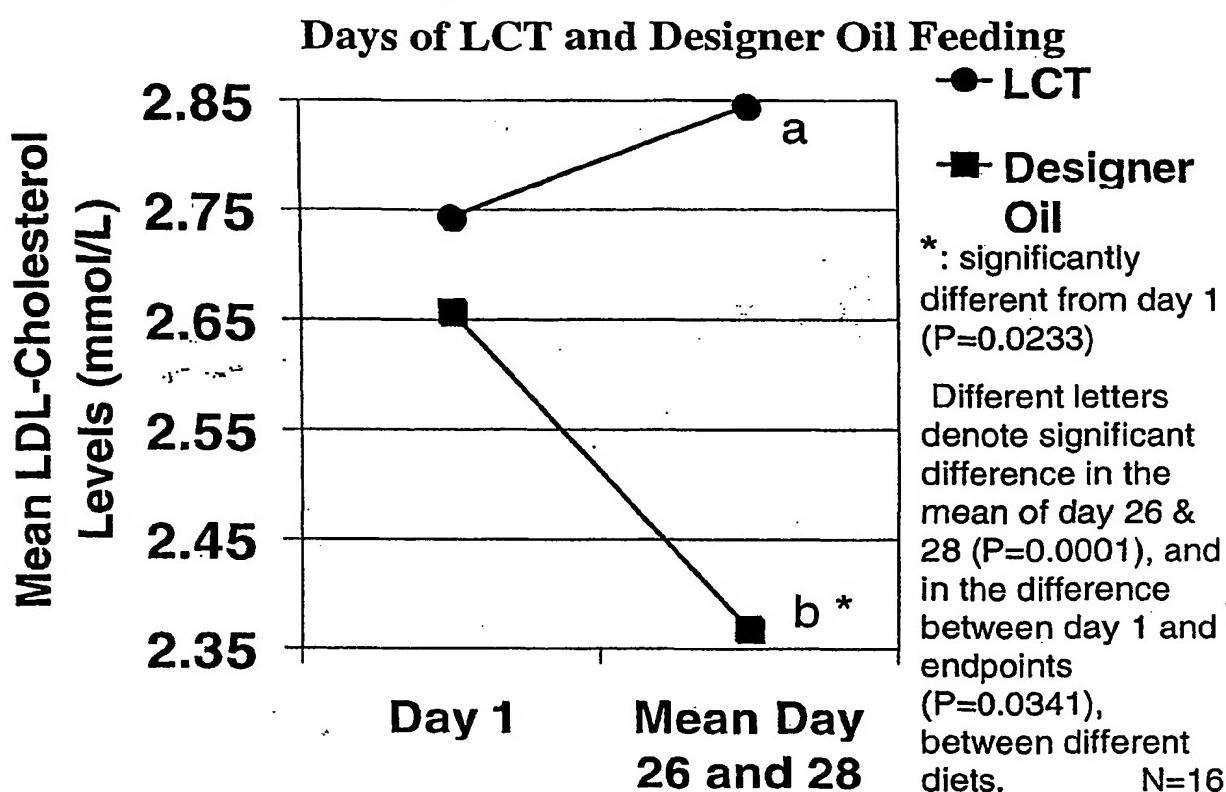


Figure 24: LDL-Cholesterol Absolute Levels After 28

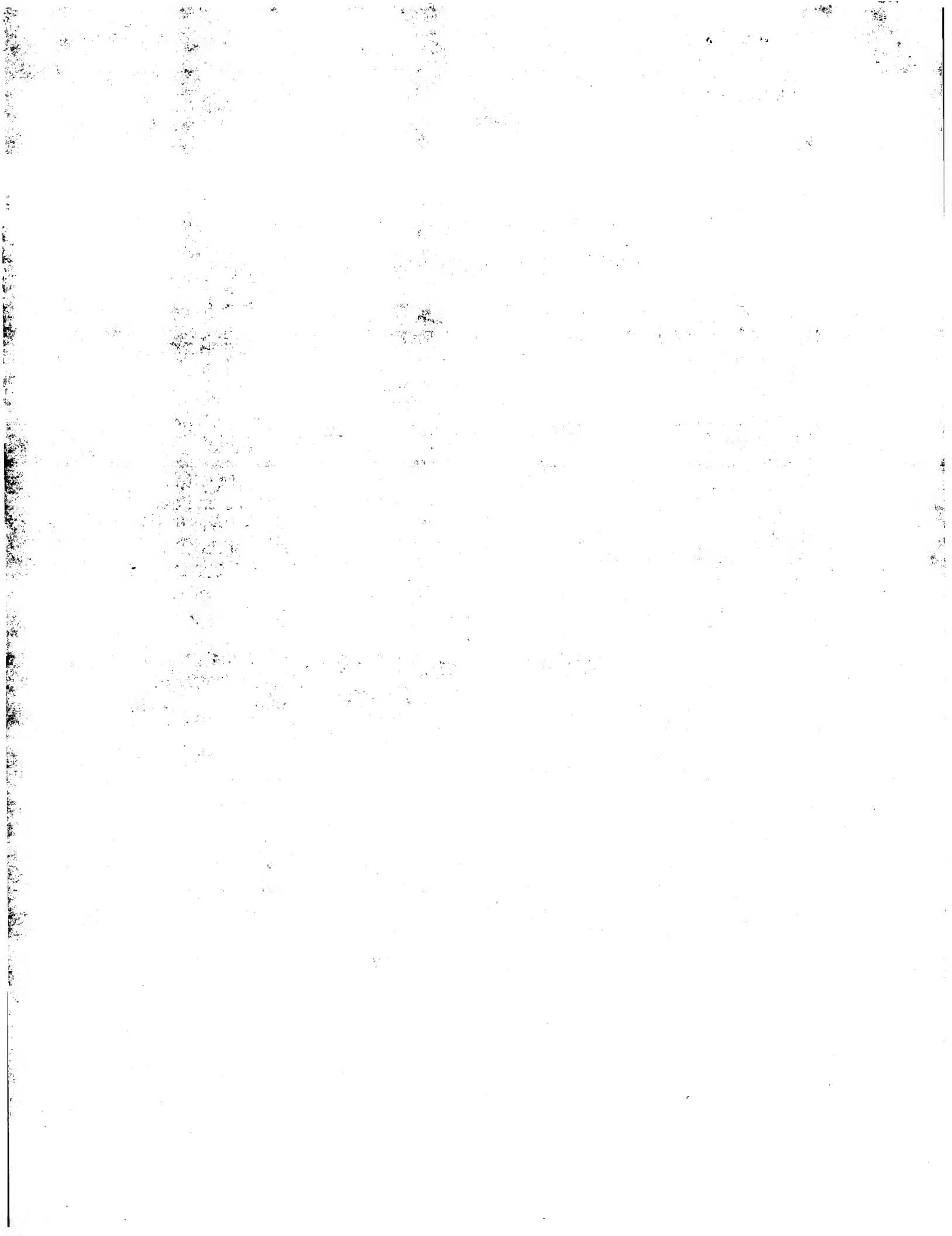
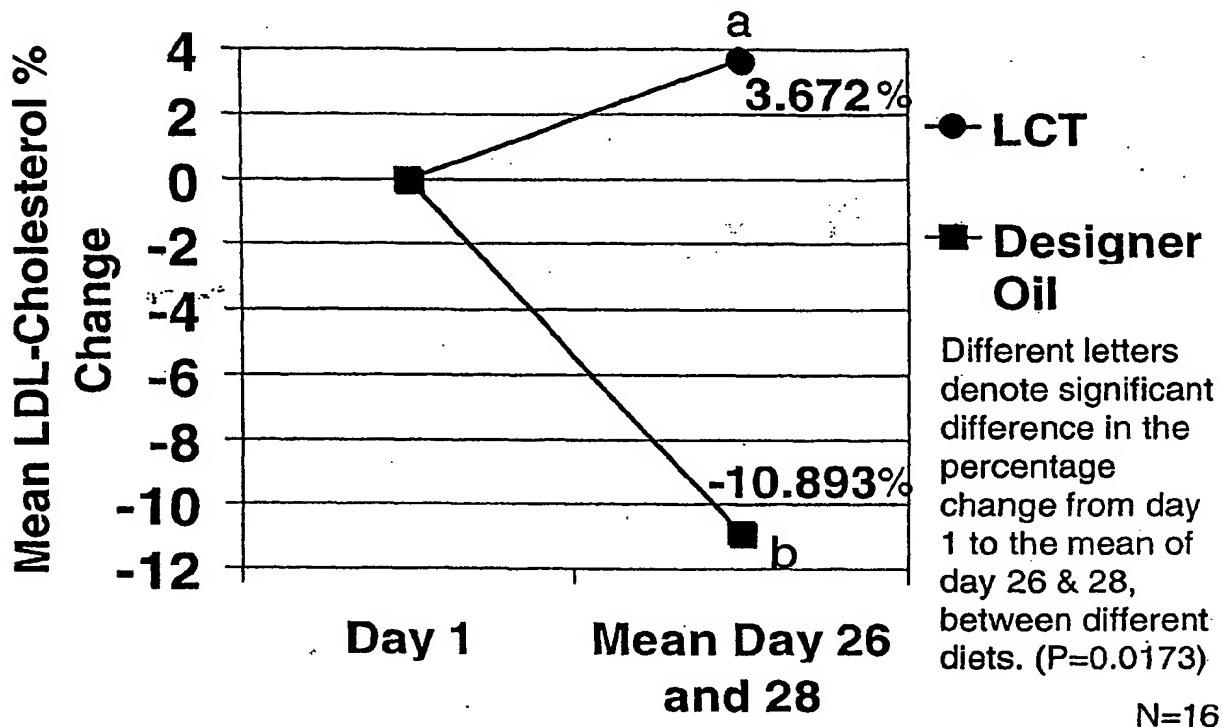


Figure 25: LDL-Cholesterol Percentage Change After 28 Days of LCT and Designer Oil Feeding



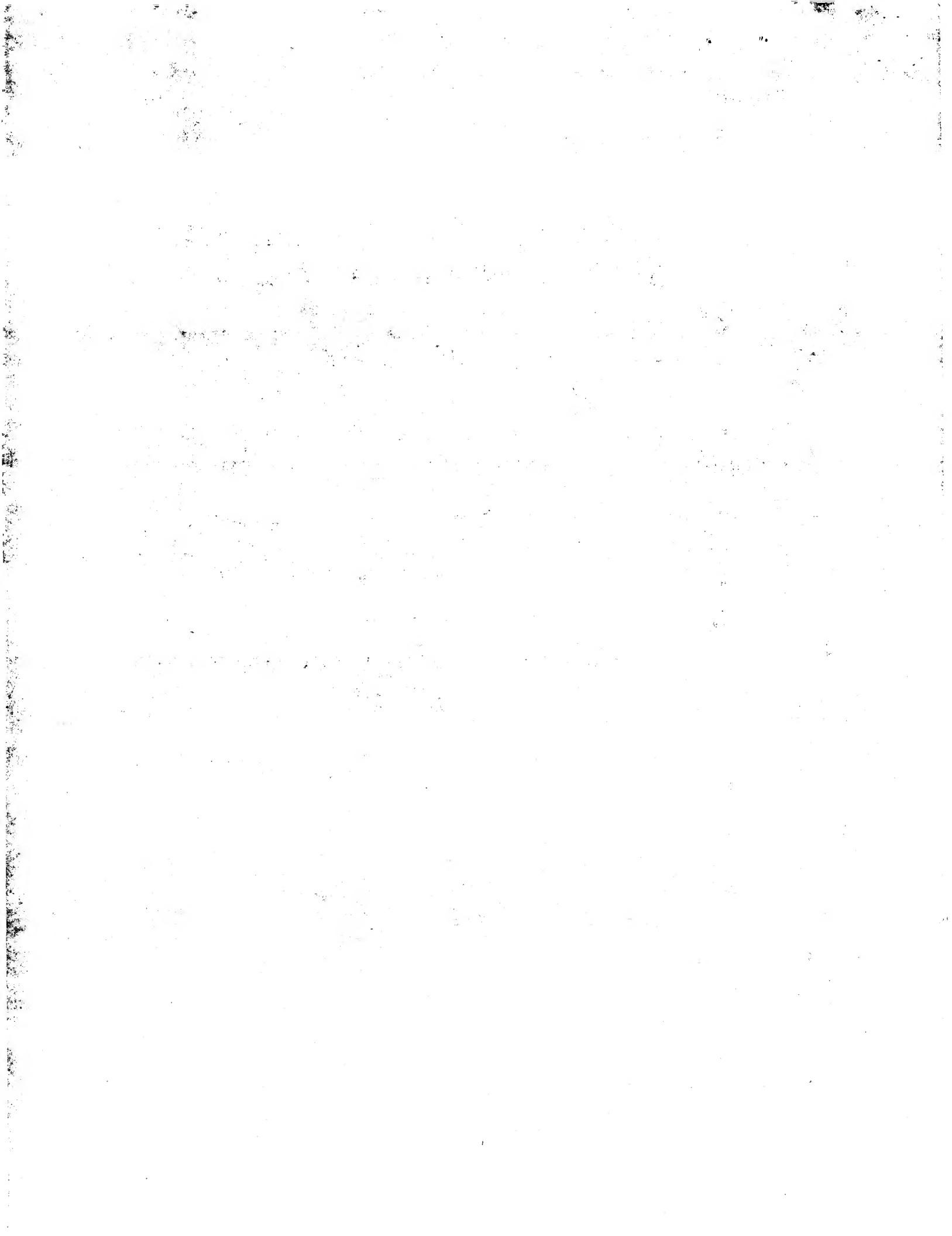
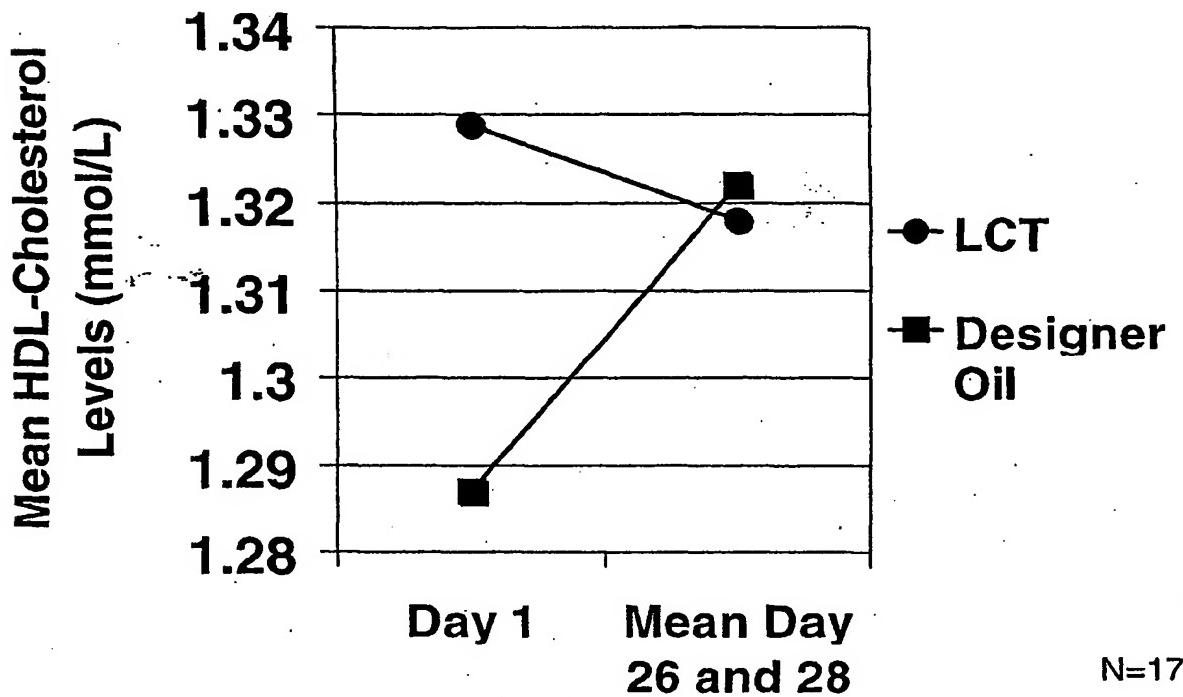


Figure 26: HDL-Cholesterol Absolute Levels After 28 Days of LCT and Designer Oil Feeding



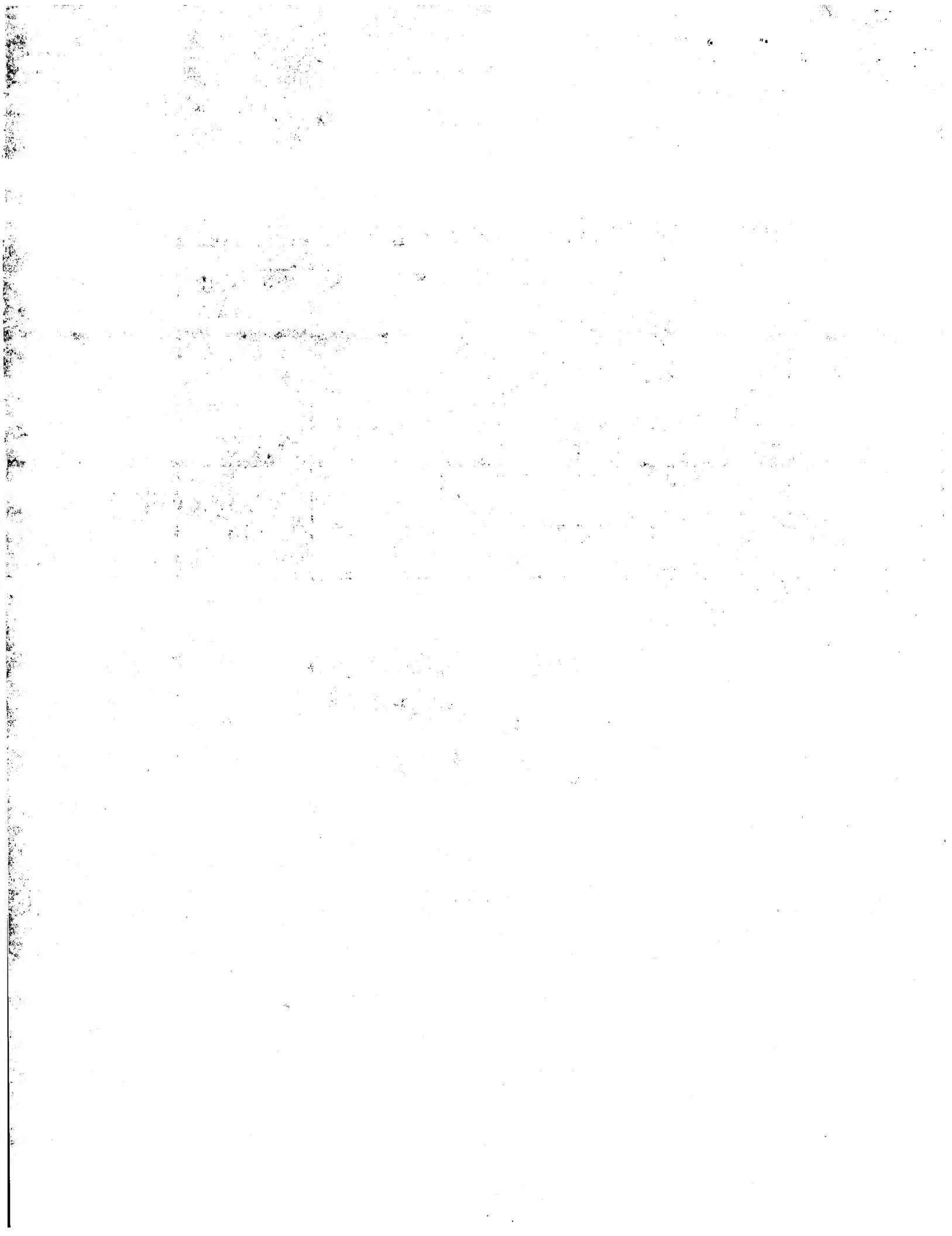
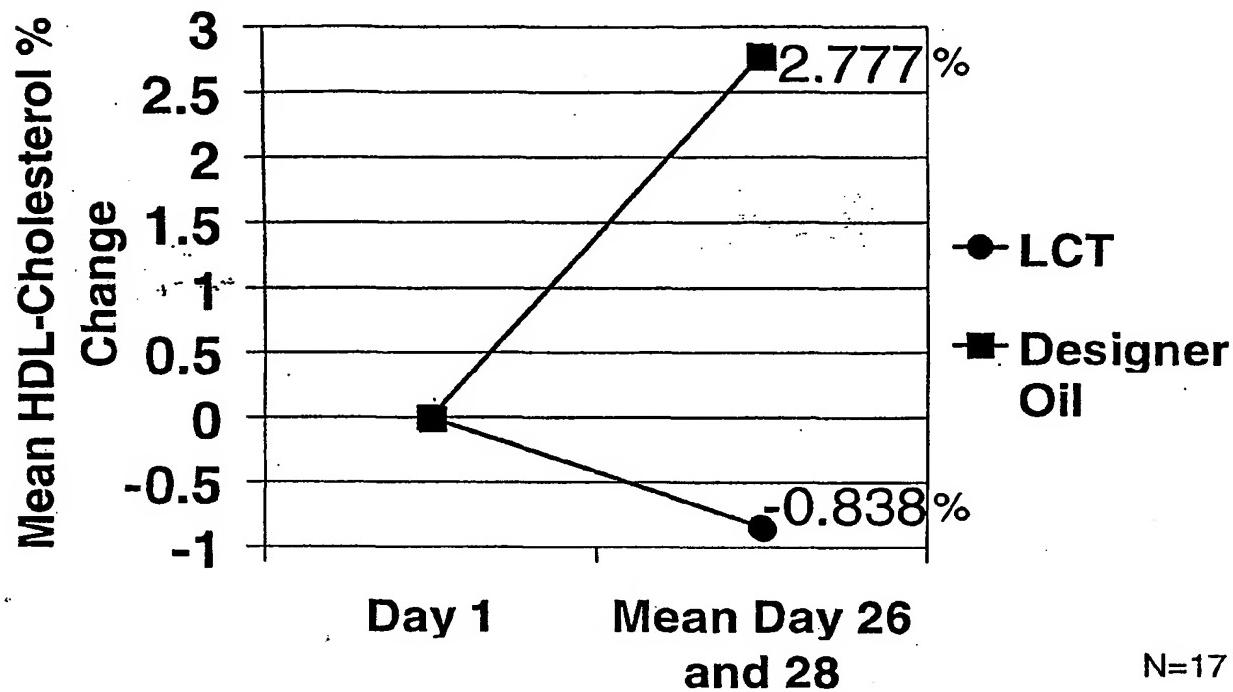


Figure 27: HDL-Cholesterol Percentage Change After 28 Days of LCT and Designer Oil Feeding



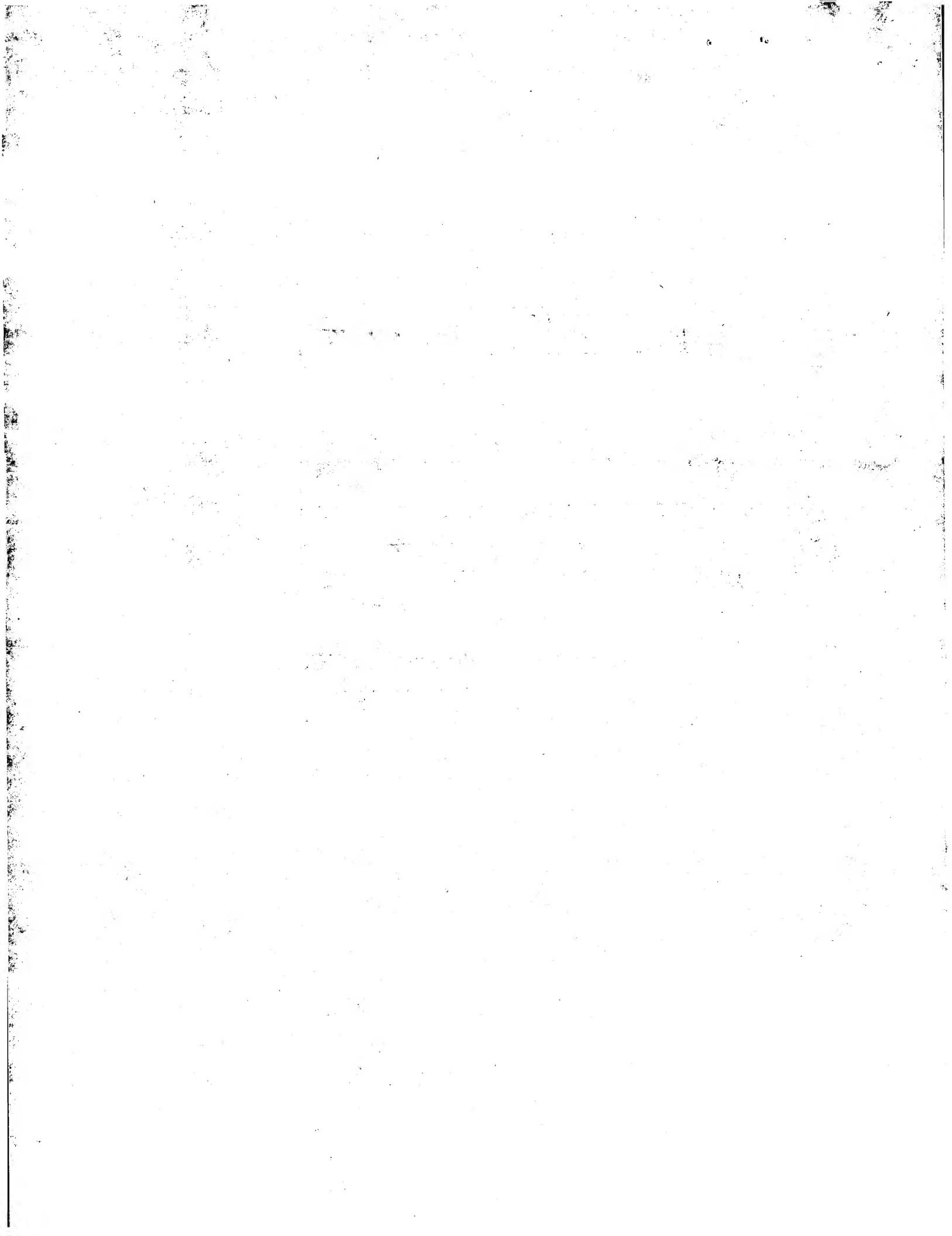
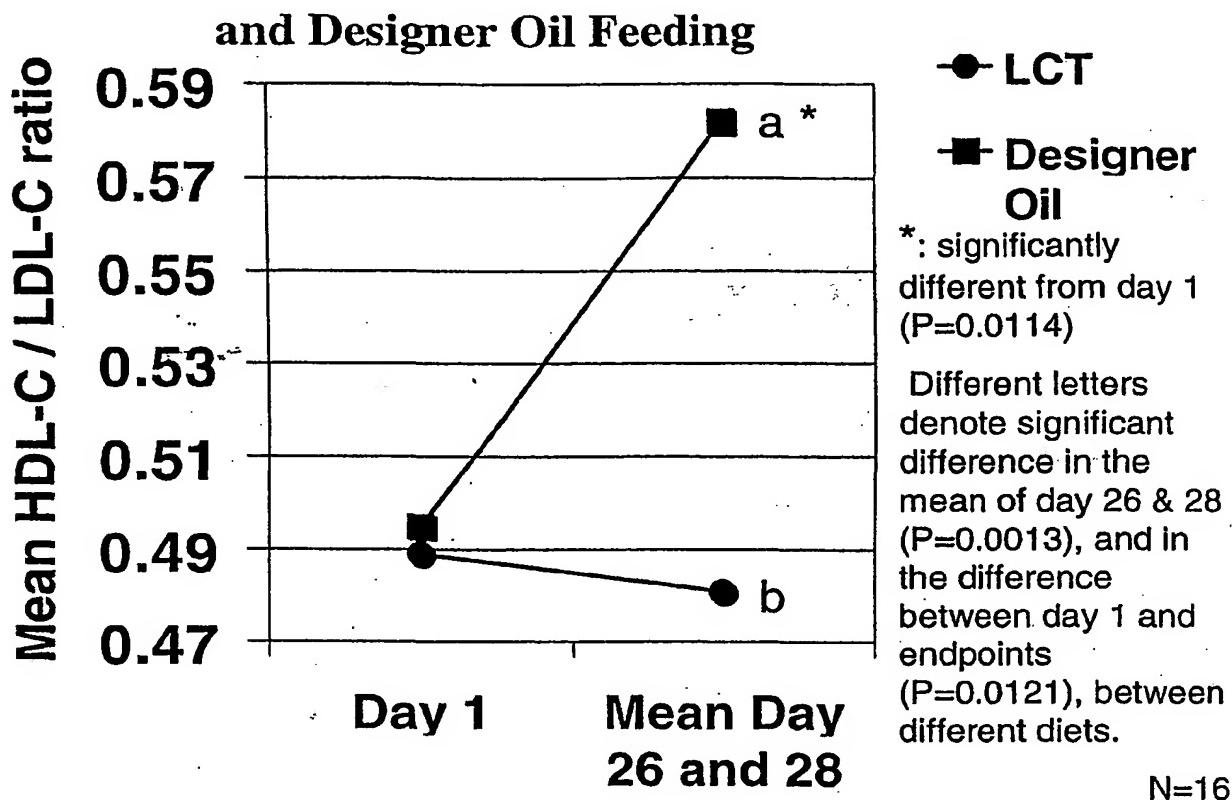


Figure 28: HDL-C/LDL-C Ratio After 28 Days of LCT

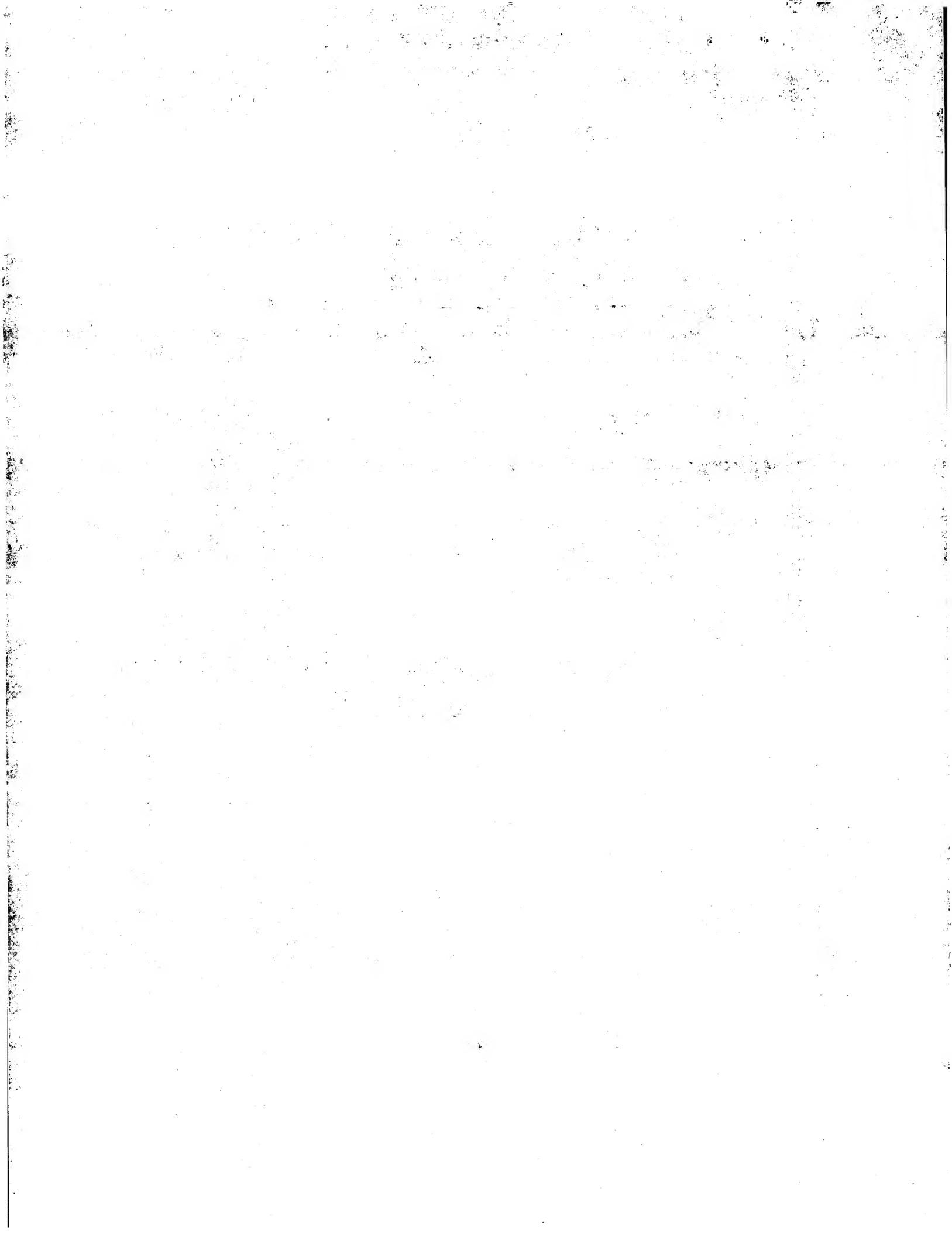
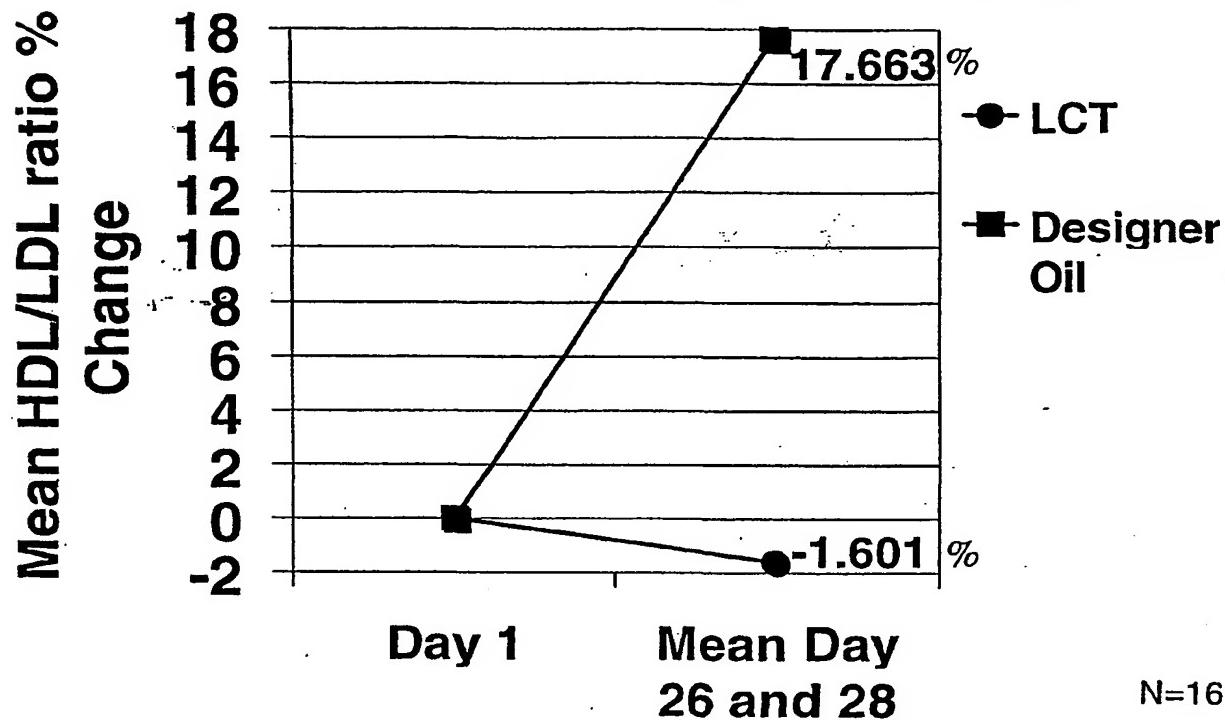


Figure 29: HDL-C/LDL-C Percentage Change After 28 Days of LCT and Designer Oil Feeding



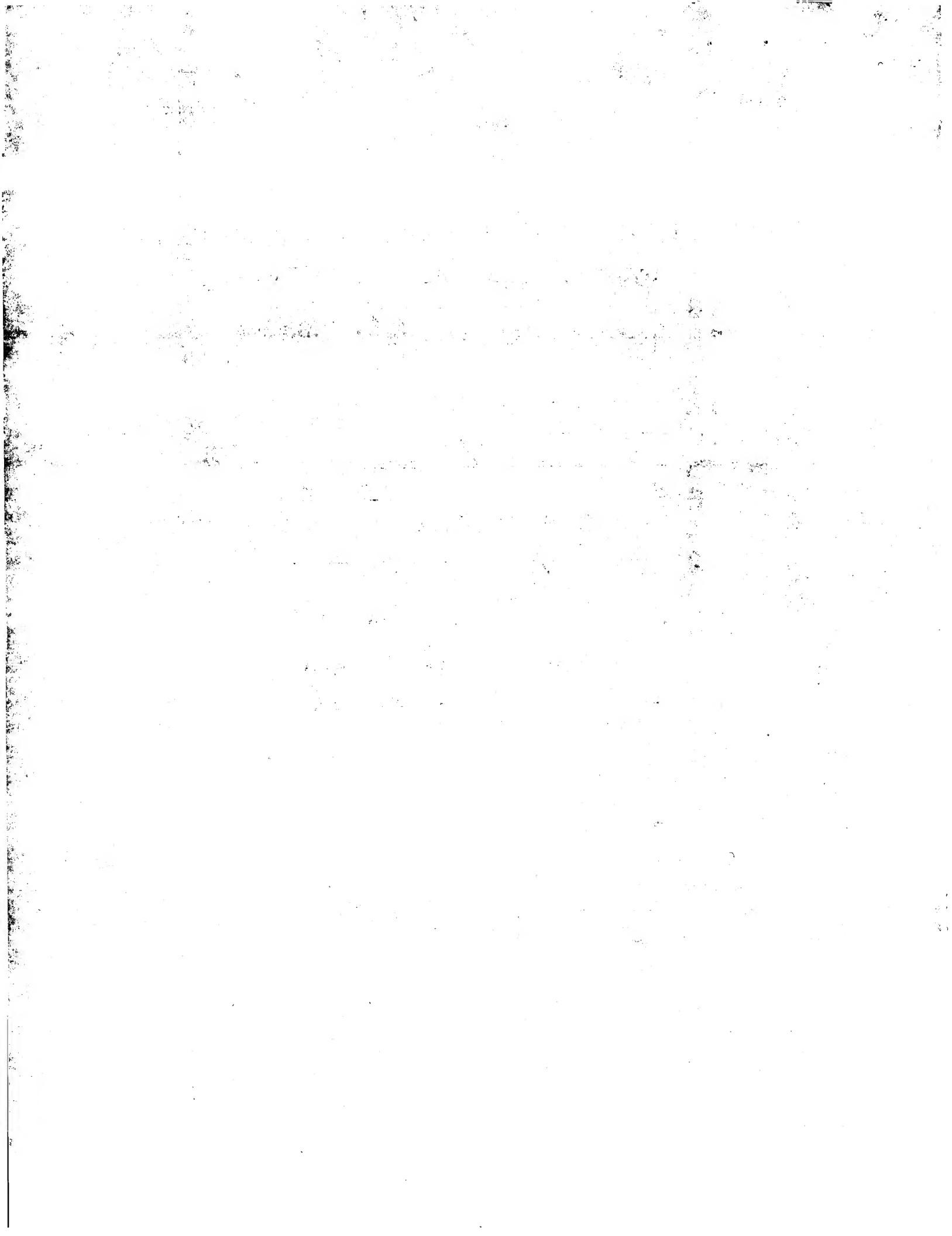
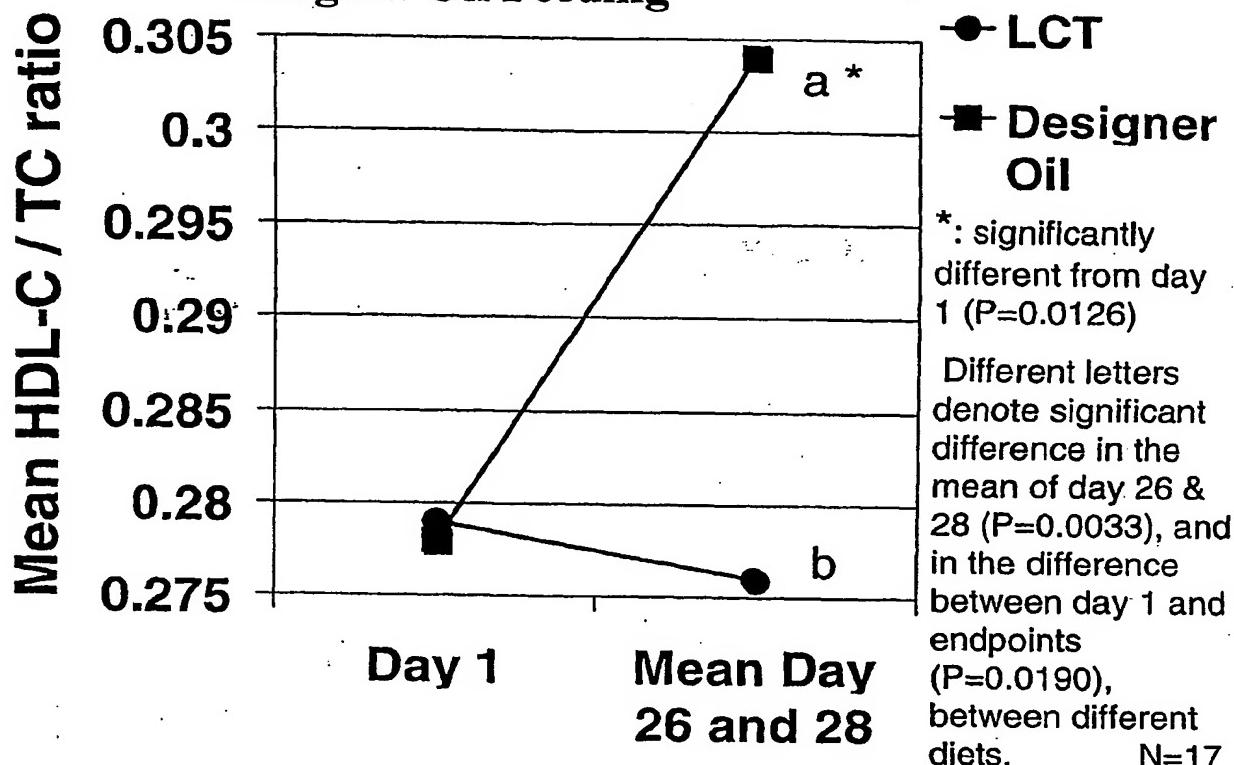


Figure 30: HDL-C/TC Ratio After 28 Days of LCT and Designer Oil Feeding



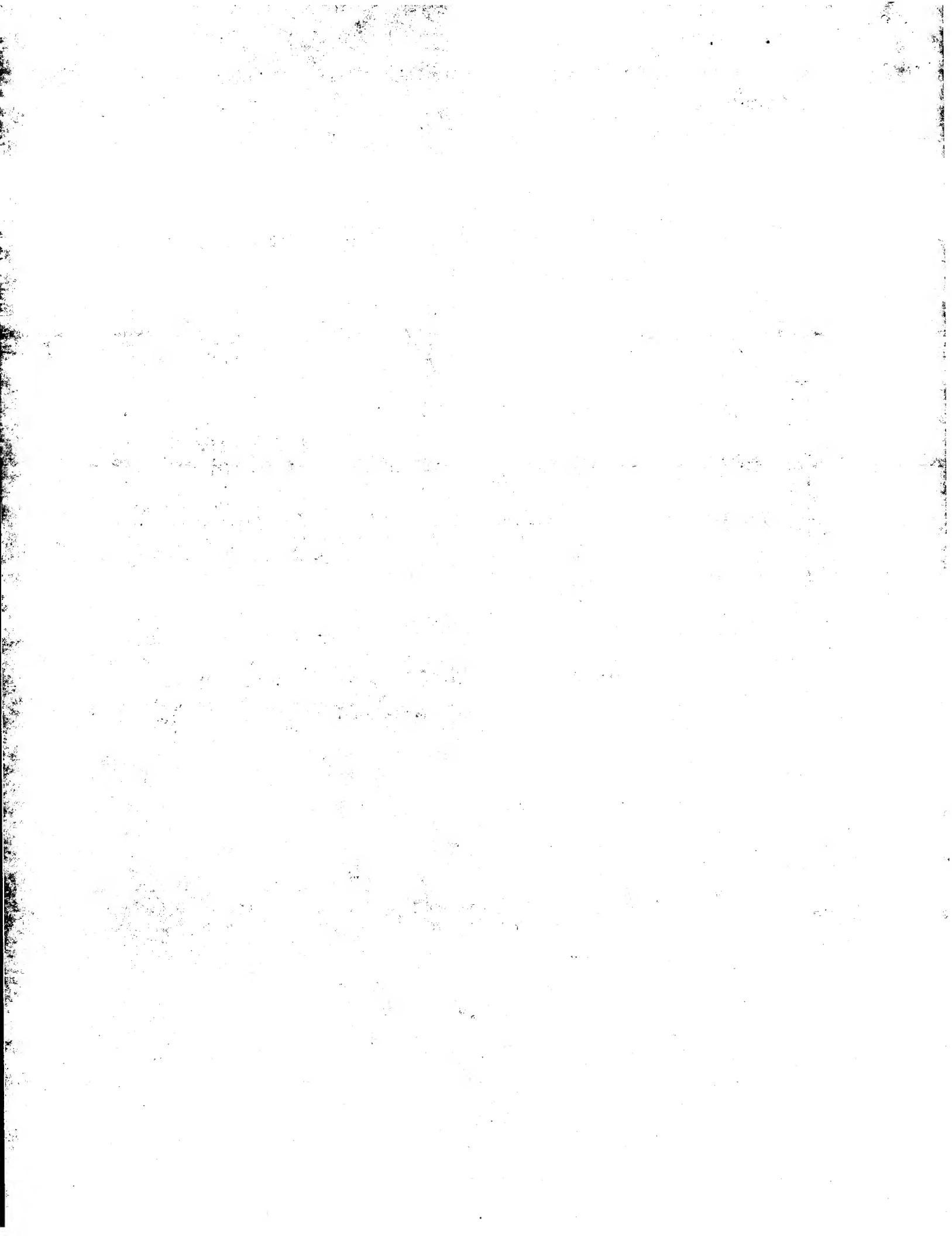
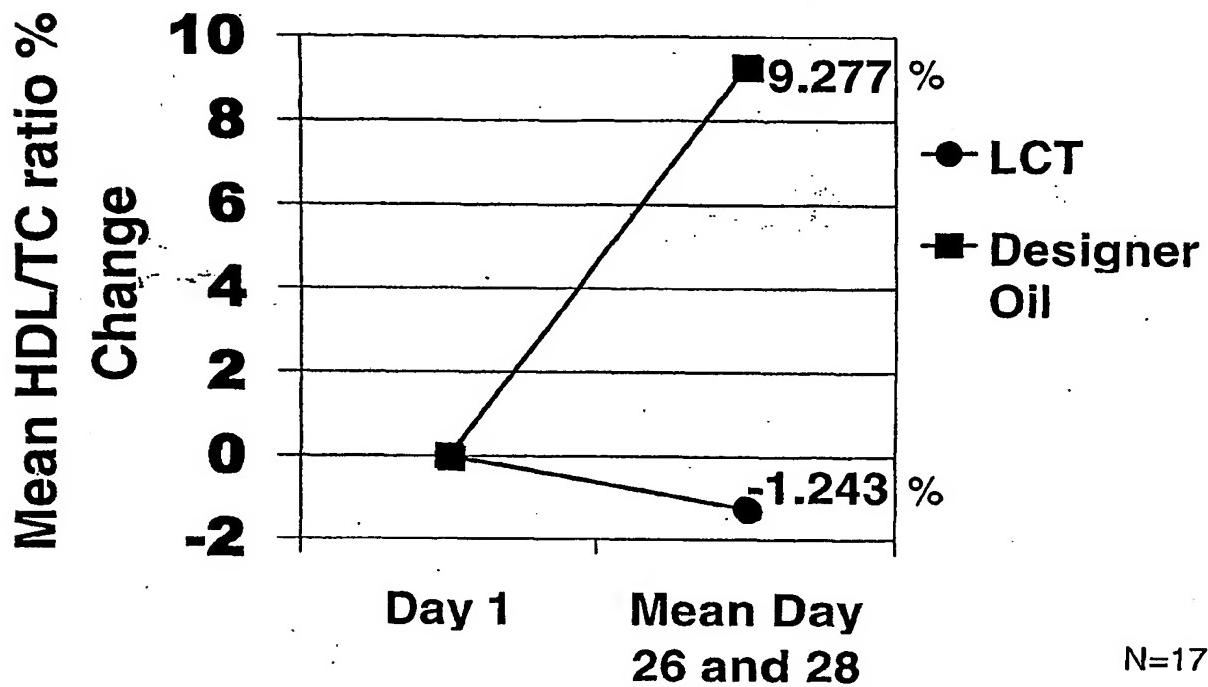


Figure 31: HDL-C/TC Percentage Change After 28 Days of LCT and Designer Oil Feeding



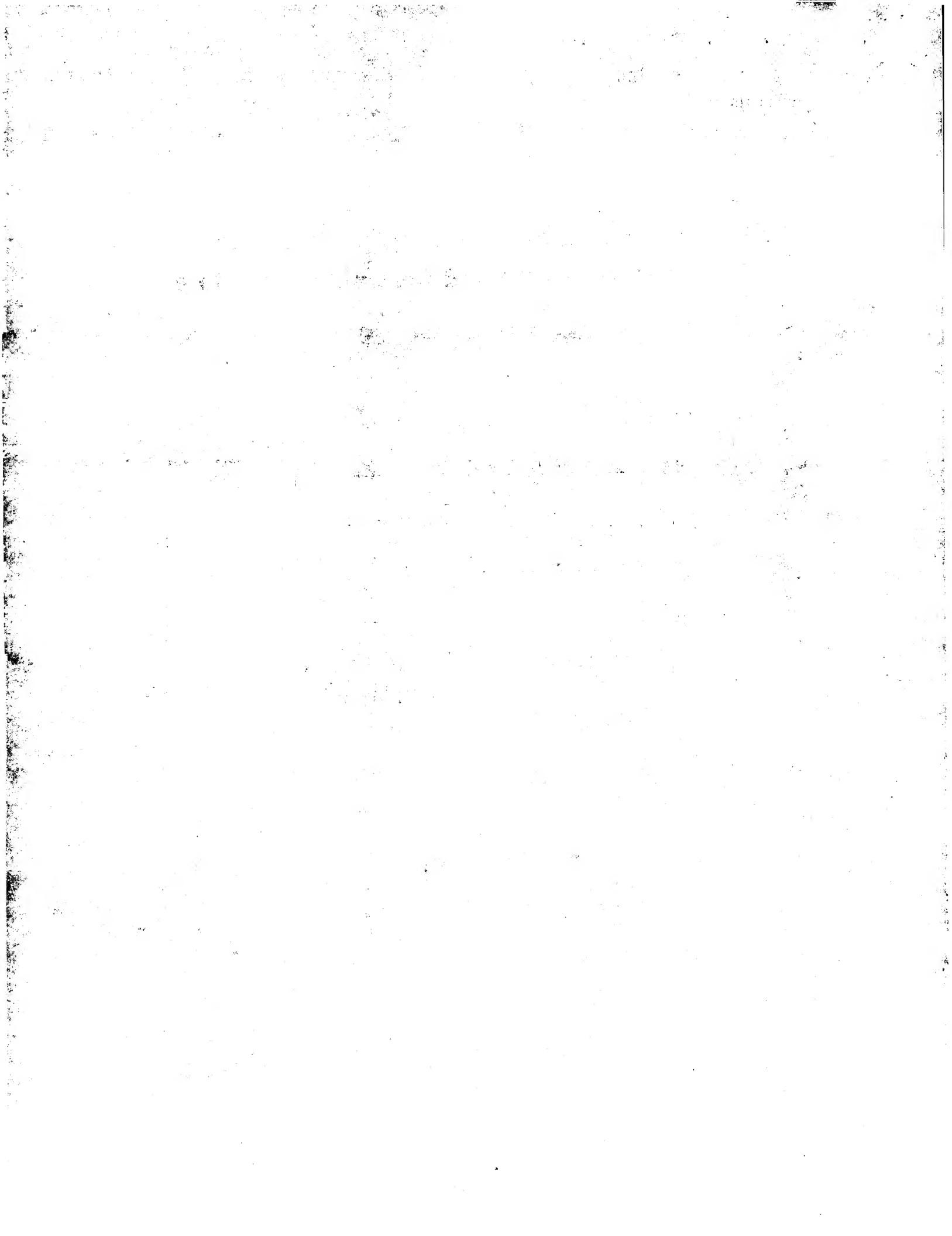
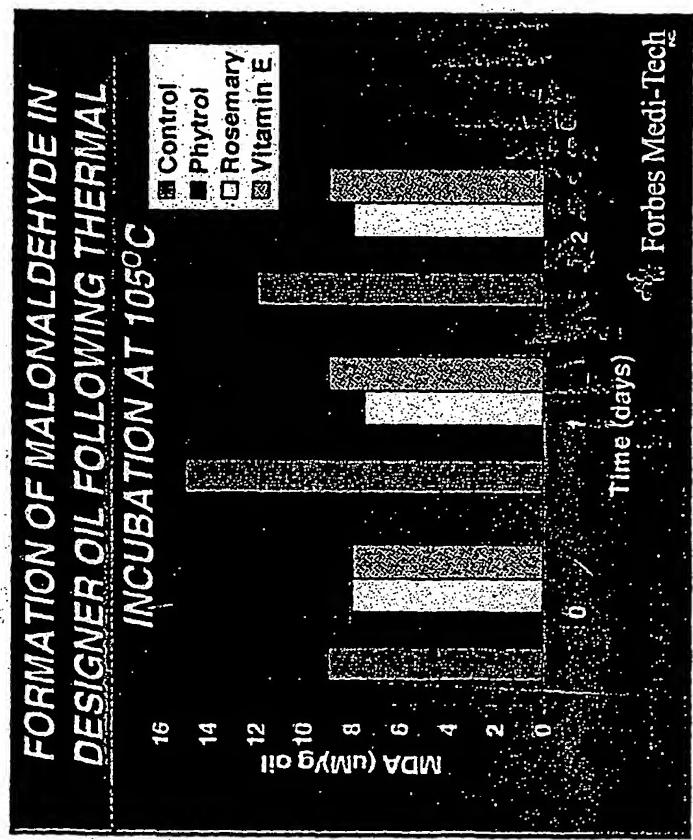


Figure 32



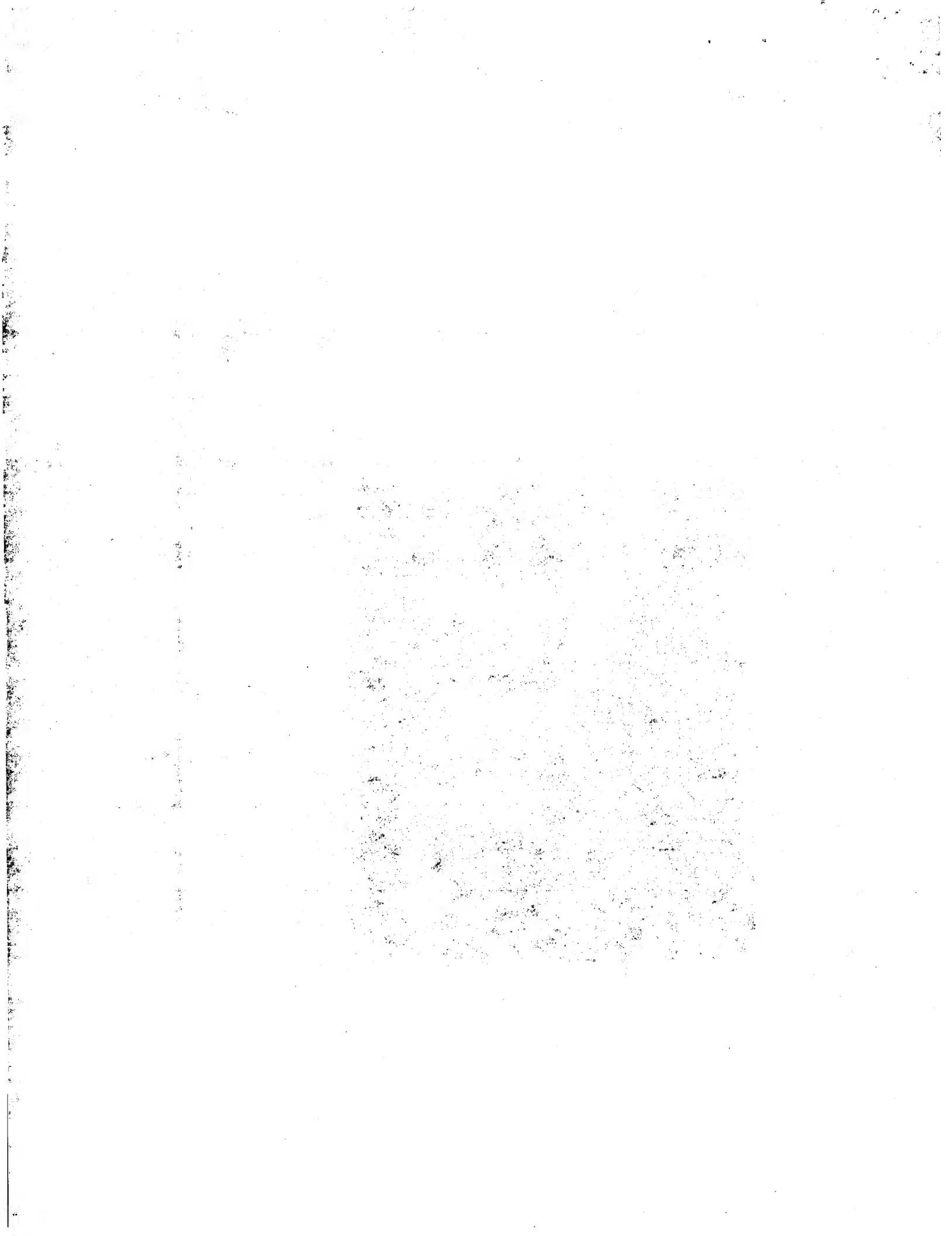


Figure 33



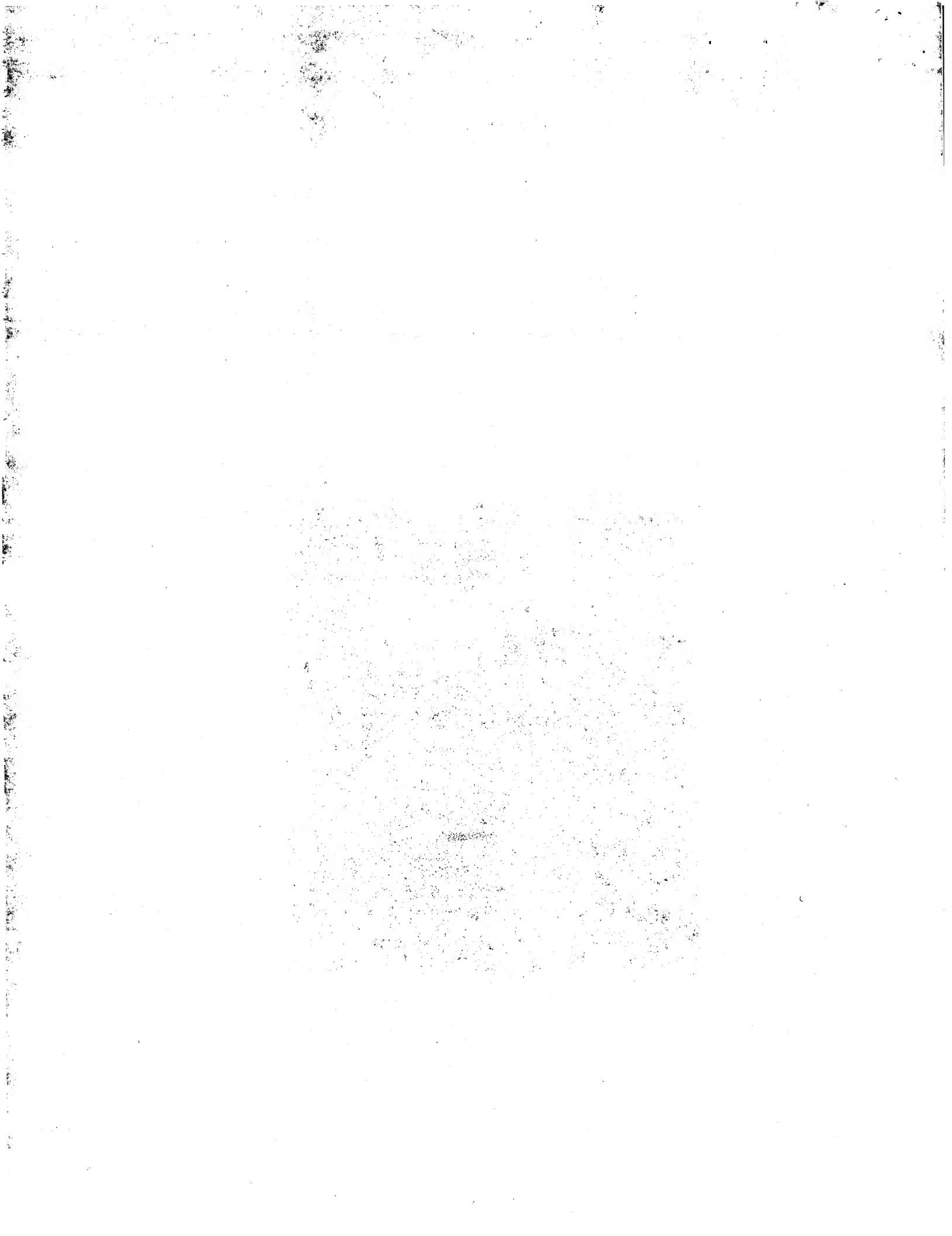


Figure 34

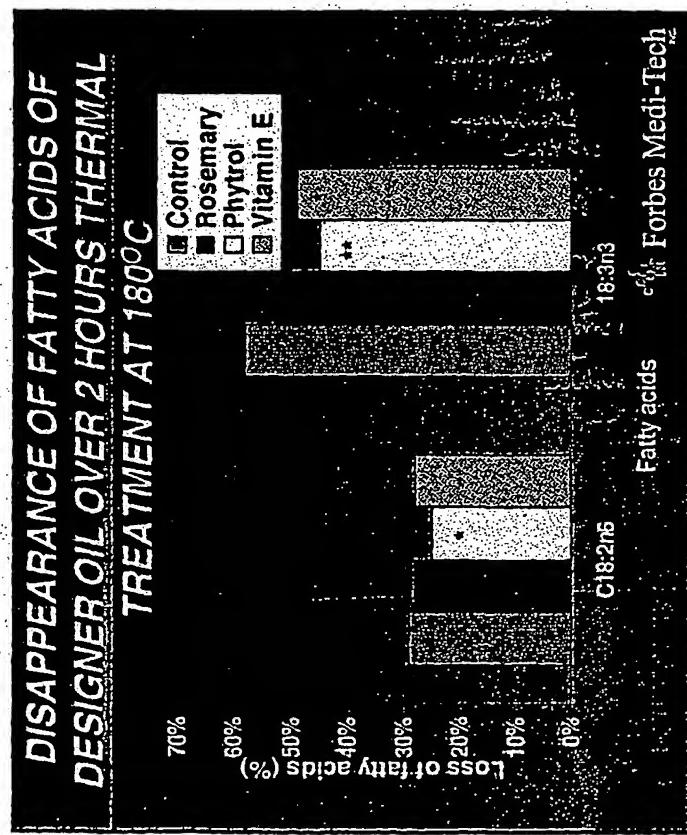
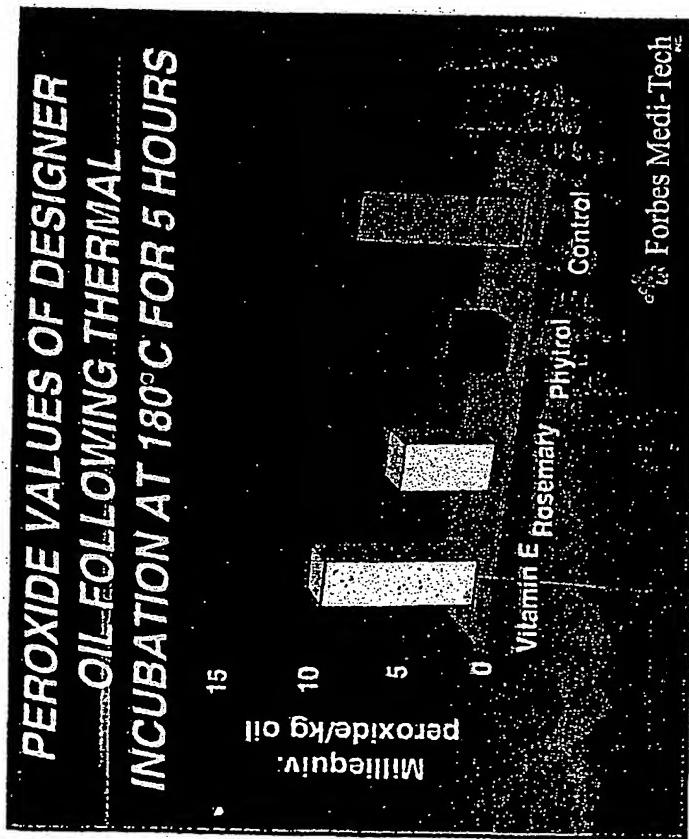




Figure 35



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